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EDITORIAL

THOUGHTS ON A NEW SESSION

By the time this issue goes to press the Schools will have entered upon another session. No doubt in most instances the occasion will be celebrated with traditional ceremony and for a period of about half-an-hour the students, old and new, will be able to gaze at a variegated assembly of caparisoned men and women collectively known as the academic staff. In all the schools the number of those holding teaching appointments has increased by leaps and bounds in recent years and it is said that there is one instance in which this number exceeds that of the students.

Whilst sophomores and even more experienced students may argue as to the identity of some of the individuals on the dais, the average fresher is filled with awe at the outward manifestation of the profundity of the discipline on which he has staked his future career. One may wonder what are the reactions of parents who are privileged to attend the ceremony. Are they torn between the Scylla of apparent value for money and the Charybdis of doubt as to their progeny's capacity to survive such an intensive academic attack?

As the magnificent panorama is spread before the tiro's untutored eyes and whilst they are still stunned by the magnitude and solemnity of the occasion a bevy of undergraduates encouraged by the plaudit of their contemporaries file obediently towards the centre of the stand to receive the customary awards for

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prowess in the previous academic year. The newcomers hold their breath in wonder-struck regard but their tense emotion may abate when they contemplate the erudite. They differ little from those who are fain to remain in their seats. Indeed the modest appearance and demeanour of those about to be honoured gives hope that they may, in due course, follow in their path and trust not to be embarrassed by squeaky shoes or a trip over the edge of the carpet.

As a rule the prizes are presented by a distinguished person who, if he be of a polite nature and accustomed to the task, delivers a homily or exhortation at the appropriate moment. These addresses have one thing in common no matter the place or occasion. The speaker always prefaces his remarks by indicating that it gave him great pleasure, and he deeply appreciated the honour, when he was invited to attend the opening ceremony and present the prizes. The second part of the address may be called the exhortation and the character of this part varies according to the speaker's knowledge of the veterinary art and science. If he is not a veterinary surgeon the theme is that of praise for a noble calling and the great work that the members of the profession do for the Country and Empire. If he be a veterinary surgeon the rhetoric may be not so flamboyant and the play of words concerns the alma mater, the wisdom of retaining the students' approach to knowledge throughout life, and the rectitude of abiding by a strict ethical standard.

When the assembly has been dismissed it is obvious that the newcomers have been impressed for they walk quietly about with a solemn air and talk to one another in low tones. No doubt their inner thoughts soar to an ethereal plane, for they know not what is yet to come. Their ecstatic mood surpasses temporarily that of those sophisticated by experience who, with loud clatter and a babble of tongue, storm the refectory with piercing clamour.

Each year as October comes and the earnest pristine students assemble, memories of the hopes and dreams of such a day long years ago are recalled. Did we exhibit the same signs and symptoms on that distant day when we embarked on our chosen career? Did we tread lightly and look with awe upon those about to be our mentors? Circumstances have changed but as all things are relative to environment the answer must be "Yes." It would be interesting to know if the teachers of to-day look as old and stern and sage as did those of yesterday and if the students have a different or better appreciation of the vocational value of the various subjects which beset their path to the final goal. In one way modern undergraduates are at an advantage. They are versed in the rudiments of the language of the pre-clinical science subjects and they can follow their teachers with some understanding from the word go whereas most of their forebears were launched suddenly and unsuspectedly on an unknown sea quite foreign to their comprehension.

Be this as it may, the old ones can treasure a memory that is denied to the young and which we would not exchange for any academic wit. It is the music of horses' hoofs which reverberated from the quadrangle.

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GENERAL ARTICLES

THE PATHOLOGY OF SOME TYPES OF PNEUMONIA AND ASSOCIATED PULMONARY DISEASES OF THE CALF

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CALF pneumonia is, economically, one of the most important diseases of cattle and it is a regularly occurring subject in veterinary literature (Jennings and Glover, 1952, and Jarrett, 1954*a*). Most of the contributions are concerned primarily with causative agents and little attempt has been made to subdivide the complex into various morphological entities. The fact that several very different pathological processes are involved indicates a probable multiplicity of ætiological factors and the nature of these changes helps to explain the marked differences between the classical clinical signs of pneumonia in the human subject and those commonly found in cattle. It is the purpose of the present work to describe in detail several types of pulmonary disease and to suggest a classification on a morphological basis.

It is realised by the writer that this classification is incomplete since it is based on personally studied material only and that a classification based on morphology alone is insufficient since different pathogens may give rise to the same pathological picture and different stages in the pathogenesis of one disease may be morphologically distinct.

Material studied.

The original basis of this work was a series of 100 consecutive necropsies carried out on calves submitted to the laboratory for diagnostic purposes by veterinary surgeons. Of these 100 cases, 67 showed pneumonic lesions, although in only 52 cases was pneumonia considered to be the major factor concerned in the illness. Since then, an extended field and experimental study of several hundred cases of pneumonia has confirmed the validity of the original classification, although several other types have to be added. Two methods have been adopted for the purpose of description and illustration, either a typical case or a stage by stage development of the lesion being described.

Pneumonia Associated with "White Scour"

Of the original 100 necropsy cases, 36 were diagnosed as white scour and 15 of these showed pulmonary lesions. The latter ranged from focal changes seen only microscopically to pneumonias of lobar dimensions.

(*a*) *Focal lesions.* These were found both alone and in conjunction with other lesions. They appear to be among the most constant findings in calfhood septicæmia and consist of small areas of thickening and necrosis in the wall of an alveolus; associated with the necrosis is a focal increase in neutrophils and septal cells. Bacteria can sometimes be demonstrated and this suggests the start of

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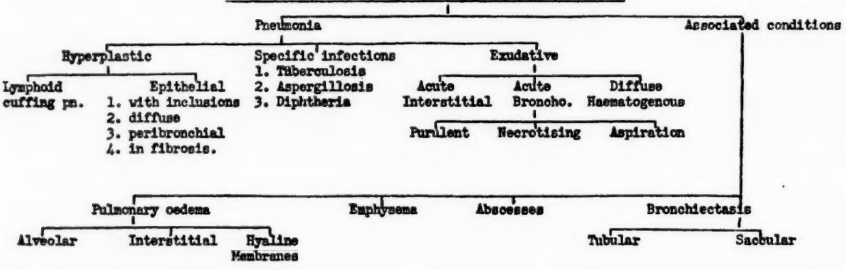
localisation of the infective agent from the blood stream. The lesions vary widely in number from case to case but occur often in areas of congestion and partial collapse (Fig. 1). The bronchial system is unaffected.

(*b*) *Diffuse interstitial infiltration.* The salient feature is a diffuse increase in number of polymorphs and mononuclears in the alveolar interstitium (Fig. 2), inflammatory cells being infrequent in the lumina of both alveoli and bronchioles.

Table 1

A Classification of the Pulmonary Diseases of the Calf



(*c*) *Early consolidation.* The alveolar walls are diffusely infiltrated with polymorphs and there are many areas showing varying numbers of these cells in alveoli (Fig. 3); bronchiolar infiltration is not a feature. Macrophages are few in number and there is no deposition of fibrin.

(*d*) *Frank pneumonia.* The pneumonia is of lobar distribution and consolidation of the classical type is present. The pulmonary capillaries are very congested and this accounts for the thickened alveolar walls; there is no marked cellular infiltrate into the walls. The alveoli are filled with polymorphs, but there is neither fibrin deposition nor obvious necrosis. The changes found in the specific pneumonias described later are absent; there is no epithelialisation, giant cell formation or septal lymphatic dilatation. The bronchiolar lumina contain polymorphs and here again there is no necrotic debris. The bronchial epithelium is intact and there are no inflammatory changes in the walls.

It is not possible to advance a definite hypothesis of pathogenesis based on these findings in field cases, but they suggest that the pneumonia often associated with scour may sometimes be an integral part of the disease and not merely a secondary pneumonia in a debilitated animal. The focal necroses may be caused by localisation of organisms in a septicæmia, the lesion then progressing through diffuse infiltration of the alveolar walls to invasion of the alveoli by leukocytes.

The other pneumonias described below may also complicate outbreaks of white scour, since the latter often produces animals of low resistance to infection.

Bronchopneumonia

This term is applied here to the pneumonias in which a bronchitis or bronchiolitis is associated with "typical" acute inflammation of surrounding alveoli. The pneumonias associated with proliferative changes such as peri-

bronchial lymphoid hyperplasia or epithelialisation of alveoli, although related to bronchi or bronchioles, are described under separate headings.

(*a*) *Acute Purulent Bronchopneumonia.*

The individual variation in morphology found in this group is great and possibly indicates that more than one type exists; it may also be that there is no sharp line of division between some of the cases in this group and those of the next, acute necrotising bronchopneumonia.

In general, the factors which the cases in this group have in common are: obvious initial localisation of the acute inflammatory process to the bronchi and peribronchial area; no widespread necrosis of the bronchial structures; little evidence of origin in the vascular channels (c.f. interstitial pneumonia); the inflammatory changes are of the normal exudative type

The cases may be subdivided into three main types.

Type 1.

Subject. Ayrshire heifer calf, age 8 weeks.

History. No clinical history was available. The farmer noticed only diarrhœa a few hours before death occurred.

Post-mortem findings. The lesions were confined to the lungs. The greater part of both lungs was congested. The left lung showed consolidation of the posterior border of the apical lobe and complete consolidation of the cardiac and diaphragmatic lobes. The hepatised tissue was slightly increased in volume, dark brown in colour and of friable consistency, and selected portions sank in water. The major bronchi in this part did not contain pus but only white, frothy fluid. Pus could be expressed from the bronchioles. The right lung showed only scattered consolidated lobules; most of the parenchyma was crepitant and contained air. The broncho-mediastinal lymph nodes were congested but were not appreciably enlarged; the normal pattern of cortex and medulla could be seen.

Microscopic appearances. (1) Non-consolidated areas. The bronchi are normal and most of the bronchioles are free of exudate. The alveolar capillaries are very congested and several small intra-alveolar hæmorrhages are present. Several small inflammatory foci are present and in these areas both the bronchioles and surrounding alveoli are filled with polymorphs. Necrosis and deposition of fibrin are not features. (2) Consolidated areas. The larger bronchi occasionally have clumps of polymorphs pressed against their lining epithelium, but the latter is intact, normal in type and shows no infiltration. The rest of the bronchial wall is normal. The smaller bronchi and respiratory bronchioles are completely plugged by inflammatory cells (Fig. 4). which are mainly polymorphs and occasional mononuclear macrophages. The cell morphology is clear and fibrin and necrotic debris are absent. The epithelium is intact and the wall itself is not invaded by inflammatory cells.

The alveolar capillaries are congested and there are many small areas of hæmorrhage involving from 10 to 30 alveoli. Congestive collapse is not a feature. Although almost every lobule shows inflammatory change, the degree of the latter varies from lobule to lobule. In some, every alveolus is packed with polymorphs, in others, only the bronchioles and peribronchial alveoli are heavily

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infiltrated, there being a much lighter cellular concentration in the peripheral areas. In some lobules, alveolar œdema is well marked, and the precipitated fluid contains a few leukocytes. Only occasional macrophages are present. These have, in H. & E. staining, a pale pink homogeneous cytoplasm and a large oval coarsely reticulated nucleus. In a few places there are alveoli filled with large foamy macrophages. At no place in the lobe is there necrosis or suppurative softening. A search was made for both eosinophilic and basophilic intra-cytoplasmic and intra-nuclear inclusion bodies without success.

The broncho-mediastinal nodes show only congestion and some sinus catarrh.

Type 2.

Subjects. Ayrshire calves, females, of unknown age, but they appeared to be unweaned (judged by size and relative degree of development of the rumen and abomasum). These cases all came from the same herd and showed the same clinical syndrome. The latter, and the pathological picture was similar to that described by Jennings and Glover (1952). The calves had been febrile and had a marked catarrhal nasal discharge and some diarrhœa. The disease ran a relatively short course and spread fairly rapidly through the calf herd, only the weakest animals succumbing. In two cases the carcase was obtained and in the other two only the thorax was submitted.

Post-mortem findings. In the two cases in which they were present, the turbinate bones were congested. The lungs were normal in volume and consistency, apart from some mottling due to patchy congestion and collapse. On the cut surface, a few of the bronchi exuded muco-pus. The lungs were slightly œdematous. It was impossible to make a diagnosis of pneumonia at autopsy due to the absence of macroscopic consolidation.

Microscopic appearances. The pneumonia in these cases appears histologically to be a mild lesion and it is difficult to reconcile the death of the calves with the degree of obliteration of air space and the damage to the lung parenchyma.

There is inflammatory exudate present in many of the bronchi and bronchioles, but few of these are plugged by it. The exudate is composed of roughly equal proportions of polymorphs and mononuclear phagocytes. There is little necrotic debris or fibrin present. The alveoli show some mural congestion but there are usually only a few inflammatory cells in each alveolus, while many contain none. There is no evidence of any hyperplastic change. Scattered lobules show complete or partial collapse with capillary congestion and absence of inflammatory exudate. There does not appear to be bronchial obstruction or any other change causing the collapse. Such areas are quite common in the lungs of calves dying from all causes, but appear to be more numerous in this type of pneumonia.

Lesions which might have caused death were not found in any other organ.

Type 3.

Subject. Ayrshire calf, female, age 4 weeks.

History. Little clinical history was available. Most of the calves on the farm were affected and several had died in the preceding fortnight. Some were

febrile, others were not, and some had a muco-purulent nasal discharge. The appetite was capricious and there was marked loss of condition. The duration of illness in this particular case was unknown.

Post-mortem findings. Lesions were confined to the respiratory tract. The apical and cardiac lobes of both lungs were consolidated, as was a strip two inches wide on the anterior border of the diaphragmatic lobes. The intermediate lobe showed consolidation of its anterior half. There was a sharp line of demarcation, corresponding to the borders of several lobules, between apparently healthy and diseased tissue.

The consolidated tissue was deep red and was of considerably greater volume than normal. The lobe edges were tense and rounded. The tissue was very friable and crumbled readily between the fingers. Lobular delineation could be seen clearly, but there was no obvious necrosis of the septal tissues. On section, the parenchymal tissue bulged from the cut surface and when pressure was applied, plugs of viscid muco-pus projected from bronchi and bronchioles and fluid flowed freely from the alveoli. Muco-pus was present in all of the anterior lobe bronchi, in the trachea and in the nasal passages; it was irregular in distribution. The turbinates appeared to be normal. The hilar lymph nodes were mildly congested and only slightly enlarged.

Microscopic appearances. The lesions are mainly confined to the areas which at autopsy appeared to be affected. Two main types of lesion are present and these are of well-marked lobular distribution.

(*a*) The bronchioles are almost or completely unaffected. The alveolar walls are thickened by tortuous congested capillaries and the alveolar lumina are filled by a homogeneous pale eosinophilic precipitated œdema fluid which occasionally contains a few strands of fibrin. The only cellular reaction is the occasional presence of a few macrophages in the alveoli. These cells have a large round or oval, coarsely reticulated nucleus, usually placed excentrically and cytoplasm which is eosinophilic and homogeneous, fatty vacuolation or phagocytosed debris being unusual.

(*b*) The second lesion, which involves the majority of lobules, appears to be characteristic of this type of pneumonia. The individual lobule shows several zones and there is little doubt that the primary and major seat of change is in the bronchiolar area. The bronchiole is plugged with a cellular exudate of polymorphs and macrophages. Nuclear outline and cytoplasmic detail are usually preserved and necrotic debris and fibrin minimal in amount. The bronchiolar epithelial lining is intact and the cellular morphology normal. In many places the cilia can be seen. The bronchiolar walls show a varying degree of congestion, but cellular inflammatory phenomena are absent.

In the immediate peribronchial area the alveoli are packed with an exudate similar to that in the bronchi. Necrosis is generally absent, but in some places there is fairly heavy fibrin deposition. The mural capillaries are tortuous and congested. In the middle and peripheral "zones" of the lobule, the cellular reaction is much less intense and is largely mononuclear in character. These macrophages are similar to those described above, their main characteristic being

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the homogeneous nature of the cytoplasm (Fig. 5). Binucleate and large multinucleated types are common (Fig. 6). Often in these areas there is precipitated œdema fluid containing fine fibrin strands. The capillaries are intensely congested.

Most of the inter-lobular septa are normal, but in some places there is dilation of the septal lymphatics and œdema of the stroma. In a few areas this process has advanced to the stage of acute interstitial pneumonia (v. infra); in this context it is interpreted as indicating that intra-pulmonary vascular spread is commencing from a lesion primarily situated in the bronchi or peribronchial alveoli.

Sections stained by eosin-phloxine-tartrazine, Giemsa and Machiavello's and Castaneda's methods failed to reveal the presence of either eosinophilic or basophilic intra-cytoplasmic or intra-nuclear inclusion bodies.

Sections of the hilar lymph nodes show reactive changes in the cortex and the presence of many macrophages, similar to those found in the alveoli, in the medullary sinuses. There is no acute inflammatory reaction.

(*b*) *Acute Necrotising Bronchopneumonia.*

The lesion which these cases have in common is an acute bronchopneumonia, in which most of the bronchi show severe damage to their walls. This is in marked contrast to the types described above where the bronchial walls were in a remarkable state of preservation.

Subject. Ayrshire calf, male, aged 14 days.

History. The exact duration of illness was not known, but was thought to have been about a week. When the calf was examined the rectal temperature was 101.5°, there was complete anorexia and copious yellow mucoid fæces were passed. There was a purulent nasal discharge, the respiration was dyspnœic, and the animal coughed frequently and showed pain when pressure was applied to the chest wall. Sulphonamide drugs were given but the calf died the next day.

Post-mortem findings. The nose, pharynx and trachea were normal and did not contain pus. There was bilateral thoracic empyema and many fibrinous adhesions were present between the visceral and parietal pleuræ. The pericardial sac contained 60 ml. of sero-hæmorrhagic fluid; there was no fibrinous pericarditis.

The left lung. A sharp vertical line divided the anterior and posterior parts of the apical lobe. The anterior half was relatively normal, whilst the posterior part was completely consolidated but showed no evidence of abscess formation. The bronchi exuded a frothy white fluid. The cardiac lobe was completely consolidated and appeared superficially to be studded with small abscesses. On section, however, there were seen to be bronchi, some of which were yellow, necrotic and crumbly, while others were filled with pus. Some of these had ruptured on to the pleura between the cardiac and diaphragmatic lobes, causing complete fibrinous adhesion. The diaphragmatic lobe showed a strip of air-containing tissue about one inch wide along its dorsal border, the remainder of the lobe resembling the cardiac lobe.

The right lung was completely consolidated and was similar in appearance to the left cardiac lobe. An abscess about three inches in diameter which was

present in the posterior part of the lobe had ruptured into the pleural cavity on the diaphragmatic surface and appeared to be responsible for the empyema.

Microscopic appearances. The majority of the lobules in the affected part show similar lesions and while the degree of affection varies, the lumina of all the bronchi are filled with a mixture of necrotic debris and inflammatory cells. In some, no cytological detail can be discerned while in others desquamated epithelial cells, macrophages and polymorphs can be seen amongst the granular eosinophilic detritus (Figs. 7 and 8). In most cases the epithelium has either disappeared (Fig. 7) or only necrotic fragments remain (Fig. 8). The bronchial and bronchiolar walls show severe damage; in some the fibro-muscular wall encloses the necrotic luminar material while in others no trace of wall remains. Immediately surrounding the damaged bronchus the alveoli are heavily infiltrated with polymorphs and macrophages and at the inner part of this area necrosis has supervened producing a fused mass of deeply basophilic pyknotic nuclei; external to this the cell morphology is distinct. The remainder of the lobule shows intense capillary congestion and a varying cytological picture although the majority are fairly heavily infiltrated with macrophages. The latter have a homogeneous eosinophilic cytoplasm and coarsely reticulated round or oval nuclei. The size and shape of the cells vary, some being large and containing 20 to 30 peripherally-placed nuclei and others having only one or two. A few alveoli are filled with fibrin but deposition of this substance is not a marked feature. In some lobules the necrotic central bronchiole is not surrounded by inflamed alveoli.

The pleura over the consolidated areas is grossly thickened and its outer surface is coated with a layer of fibrin; immediately subjacent to this the mesothelium can be seen as a row of swollen cuboidal cells often with more than one large vesicular nucleus per cell. The stromal collagen fibres are swollen and separated by fluid, the spaces so produced being irregularly invaded by mononuclear leucocytes. Both the capillaries and the larger blood-vessels are very congested but the main vascular change consists of dilatation of the pleural lymphatics, this latter accounting for most of the thickening. The precipitated fluid in these lymphatics contains some mononuclears and fibrin. This process has not extended to the degree present in most cases of interstitial pneumonia (*vide infra*).

The bronchial nodes show an increased number of macrophages in the medullary sinuses (Fig. 9) and scattered foci of fibrinoid necrosis in the germinal centres and in the medulla.

One case, for which no details of history are available, shows a much more acute process. At autopsy the lungs were congested with some consolidation of the anterior lobes. Pus, abscess formation and gross evidence of necrosis were absent. The most regular histological feature is fibrinoid necrosis of the bronchiolar wall and the surrounding alveoli; structural details of the tissue can still be seen in "ghost" outline, the affected parts having lost their normal staining affinity. The surrounding tissue is normal in some areas while in others there is infiltration by macrophages of the type described above.

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It is open to some doubt whether acute purulent and acute necrotising bronchopneumonia can be sharply separated from each other since both types of lesion are present in some cases. There is some evidence, however, that the necrotising type is much more severe clinically and has a poorer prognosis. The latter is only to be expected in view of the destructive nature of the pathological process.

Acute Interstitial Pneumonia

The term "interstitial" is commonly applied to several different types of pneumonia; e.g., it may imply reactive changes in the alveolar interstitium, in the peribronchial or perivascular area or, as the term is used here, to denote a process in the interlobular septal tissue. The choice of name for this last group is defended on the grounds that the condition is acute both clinically and pathologically, and it involves the true interstitium, i.e., the septa, as distinct from the parenchyma.

In the cases described here, interstitial pneumonia is the basic and uncomplicated lesion, but in several other types of pneumonia, areas of similar interstitial change occur and are thought to represent secondary intrapulmonary vascular spread of a severe inflammatory process.

Several animals suffering from intestinal pneumonia have been seen by me when alive, their ages ranging from five days to six years. The animal is acutely ill, febrile (105° to 106° F.), dehydrated, dyspnœic, anorexic, and may show pain when the thorax is compressed.

Post-mortem findings. As in other calf pneumonias the anterior lobes are most constantly affected, although cases have been noted in which almost the whole of the diaphragmatic lobes has been involved. The affected lobe does not collapse when the thorax is opened. It is deep red, friable and tense with rounded lobar edges and the overlying pleura usually shows acute fibrinous pleurisy; adhesions between the parietal and visceral pleuræ are common. The outstanding feature is an exaggerated lobular delineation due to thickening of the interlobular septa. The latter may be only œdematous or may be thick, yellow, dry and necrotic, depending on the stage of the process. The changes may be so severe as to give the appearance of pin-point areas of parenchyma each containing a bronchiole, surrounded by rectangular areas of coagulative necrosis; or portions of lobes, several inches square, may have undergone complete coagulative necrosis. Suppurative softening and the presence of pus in the bronchi are not common features. The broncho-mediastinal lymph nodes are usually intensely congested and may show flecks of necrosis.

Microscopic appearances. The clinical features, post-mortem appearances and the pathogenesis of the disease are easily understood from a consideration of the morbid histology. The following description is based on a series of lesions selected from different cases and from different parts of the lung in one case.

Stage (1) (Fig. 10). The subpleural and septal lymphatics are grossly dilated, the valve cusps of the former being pulled apart. The fluid in these vessels is precipitated as a smooth homogenous lightly eosinophilic film and within this very fine spicules of deeper staining fibrin are deposited in an irregular

fashion. The cellular content at this stage varies even within the same vessel. At some places there are no cells while at others, corresponding to the position of heavier fibrin reticula, there are present small aggregates of cells, mainly monocytes and lymphocytes. Neutrophil leukocytes are not present in any number. The walls of the lymphatics and the septal stroma show minimal cellular changes and only mild œdema. The adjacent tissues show only capillary congestion and occasional macrophages in alveolar lumina. The bronchi and bronchioles do not show inflammatory changes.

Stage (2) (Fig. 11). The septa have become grossly thickened and at this stage they are easily visible to the naked eye. The lymphatics are markedly distended and occluded by a fine meshwork of fibrin in which are entrapped only a few cells. The walls of the vessels are thin and uniformly eosinophilic; this, together with the loss of nuclear staining affinity, indicates incipient necrosis. The surrounding septal stroma shows œdema and separation of fibres, and here, too, there is some loss of staining affinity. This tissue contains a few neutrophils and macrophages but the cellular reaction is nowhere intense and is confined to the septa. The surrounding alveolar tissue shows only congestion and the presence of a few macrophages. The bronchi and bronchioles are normal.

Stage (3) (Fig. 12). The inflammatory phenomena are still confined to the septa. It is difficult to see any clear line between the thrombosed lymphatics which are undergoing necrosis and the œdematous stromal tissue, the fibres of which are separated and have lost their normal sharp definition, the material between them being granular and eosinophilic. A cellular reaction has now become more prominent although it is still mainly focal in character. The infiltrate is composed of neutrophils and macrophages in almost equal numbers. The alveoli and bronchi are similar to these described in Stage 2.

Stage (4). The septal tissues have undergone coagulative necrosis, there being complete loss of normal staining affinity of the formed elements (Fig. 13). The septa are of the same breadth as in Stage 3, but are now composed of an almost amorphous palely eosinophilic granular material in which can be seen some "ghost" outlining of cells and vasculature. At the lobular edge of the septum there is a narrow band of intense cellular infiltration (Fig. 14). The cells are mainly neutrophil polymorphs and their morphology is much clearer at the alveolar than at the septal side which appears to indicate a rather rapidly advancing coagulative necrosis preceded by a narrow band of acute inflammation. In the alveoli immediately adjacent to the septa there is some deposition of fine fibrin strands and a light diffuse mural and luminar macrophage infiltration. The central alveoli, bronchioles and bronchi are for the most part normal although an occasional bronchus contains a few polymorphs (Fig. 14) and some lobules show congestion, bronchitis and alveolar collapse (Fig. 12). There are no traces of necrosis in the bronchial tree.

Stage (5) (Fig. 15). This represents the final stage of the process and shows complete necrosis of the septa and of many alveoli. The surprising thing about this lesion is that, even at this stage, when the greater part of the affected lobe has undergone complete coagulative necrosis, the adjacent alveoli show a

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very minor degree of inflammatory change. Bronchioles situated close to the inflamed septa may contain little or no cellular exudate or necrotic debris. The process proceeds until there are areas of complete necrosis (Fig. 16) of up to lobar size.

The septal changes parallel those of the pleuræ and subpleural tissues so that a fibrinous pleurisy is established at an early stage in the disease.

The development of this pneumonia may be summarised as thrombosis of the lymphatics of the pulmonary septa, their subsequent necrosis and inflammation and the spread of this process in a centripetal fashion to involve the lobules. The final result is not suppuration and abscess formation, but coagulative necrosis. The bronchi are relatively unaffected even at a late stage.

The origin appears to be hæmatogenous rather than ærogenous although in most cases no primary extra-pulmonary focus of infection was found. It seems possible that the causal organism or organisms involved have a pre-dilection site in the interstitial tissues of the lungs. The initial focus of infection has been found in some cases, viz., sepsis supervening in a peptic ulcer, omphalophlebitis and omphaloarteritis. Small foci of similar pneumonic type have also been found in some cases of acute bronchopneumonia; this has been interpreted as intrapulmonary vascular spread of such a pneumonia.

Inclusion Body Pneumonia

The following is a summarised account of a description previously published (Jarrett, 1954*b*).

The affected lobes are consolidated, may or may not sink in water and the bronchi contain varying amounts of muco-pus and white, frothy fluid. The greater part of both lungs may be involved.

The basic lesion is the lining of all or some of the alveoli of a lobule by a single layer of low cuboidal epithelium. The free edge of the epithelial sheet is undulating due to the bulging of the nuclei and to focal cellular proliferation forming epithelial giant cells of irregular outline and nuclear distribution. A similar process occurs in the alveolar ducts and terminal bronchioles (Fig. 17) although there is no indication of cellular hyperplasia in the bronchi. Many of the epithelial cells of the alveoli and bronchi contain intracytoplasmic inclusion bodies usually lying at the poles of the nuclei or between the latter and the basement membrane. The inclusion bodies are strongly eosinophilic and retain their colour when all dye has been washed out of the erythrocytes. While stained most satisfactorily by the eosin-phloxine-tartrazine method, they are easily seen in hæmalum and eosin, picro-Mallory and in Romanowsky preparations; of the latter, dilute Giemsa is best and it also gives delicate staining of the proliferated epithelium and giant cells. The inclusions are not stained by Machiavello's, Castaneda's or the periodic acid-Schiff method. They range in size from 1 to 6 μ with an average diameter of 3 μ. They appear homogeneous in paraffin sections and are confined to the cytoplasm. The morphology and staining reactions of these bodies is similar to those of measles, canine distemper and virus pneumonia of infants.

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Superimposed on these changes there is usually a light diffuse infiltration of polymorphs.

A full discussion of these findings has already been given (Jarrett, 1954*b*) and their implications may be summarised thus: (1) there is a close similarity between the histological picture and those of human measles, giant cell pneumonia of infants and canine distemper, all proven virus infections, and also to a pneumonia of the cat seen by the present author but not yet described in the literature. It is not valid to deduce etiology from morphological appearances but the latter are suggestive of virus infection; (2) in measles and distemper the characteristic virus pneumonia may become obscured by purulent changes. It seems possible that the same may happen in the calf and that some of the bronchial or confluent pneumonias of the "'typical" or exudative variety can be superimposed on an earlier, epithelialising lesion.

Other Epithelialising Pneumonias

These pneumonias have already been described (Jarrett, 1954 *a* and *b*; Jarrett, *et al.*, 1954). They may be broadly classified into three main groups:

(1) The alveolar epithelialisation is confined to that part of the lobule immediately around a bronchus or bronchiole. The air-spaces are lined by a regular cuboidal epithelium which shows little tendency towards bizarre hyperplasia. The alveolar walls are usually thickened and separated by young fibrous tissue and signs of acute inflammation are absent. A similar picture has been produced experimentally (Watts, *et al.*, 1948) by injecting corrosive fluids into the tracheas of small laboratory animals and it seems possible that such lesions in the calf have their origin in bronchial trauma, e.g., in parasitic bronchitis. Inclusion bodies have not been demonstrated in the epithelial cells in the bovine cases. The surrounding alveoli are usually of normal configuration.

(2) This type is thought to be of great importance both in young and in the adult cattle. It is often associated with the loosely-defined clinical syndrome of fog fever, i.e., sudden onset of severe dyspnœa, pulmonary œdema and emphysema with subsequent collapse of the animal. At autopsy, in addition to pulmonary œdema, the anterior, lobes and often part of the diaphragmatic lobes, show a peculiar type of consolidation. On opening the thorax the lobes do not collapse to the same degree as normal lung since there is still a fairly high content of air and therefore crepitation may be present. If œdema is not too severe, selected portions float in water. (It is worth while noting that in many cases of calf pneumonia, consolidated portions do not sink; this is possibly in part due to the mild interstitial emphysema which is often present.) The pleura is glistening, the affected lung tissue is of light plum colour and feels like rubber. Pus is not usually present in the bronchi.

Microscopically there is diffuse alveolar epitheliatisation (Fig. 18). The epithelium is fairly regular, cuboidal or low columnar but occasionally shows proliferation to form small "giant cells." In some lobules all alveoli are affected; in others only those adjacent to the septa. This distribution seems to favour the view that there is normally some epithelial tissue in alveoli since it

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can be shown by serial sectioning in these bovine cases that there is often no direct connection between bronchiolar and alveolar epithelium. There is no alveolar mural fibrosis and this, together with the clinical picture and the type of epithelium, suggests that the whole process is of a relatively acute nature.

Most cases are associated with *Dictyocaulus viviparus* infestation while in some no definite connection with lungworms has been demonstrated. The etiology of this peculiar reaction is obscure but pilot experiments have given some indications as to its possible cause and a large experiment is in progress to investigate its connection with different patterns of lungworm infection.

(3) In lobes affected with bronchiectasis there is sometimes marked fibrosis around the bronchi and septa so that the lobule is encroached upon and only a few alveoli remain. These may be lined by cuboidal epithelium and may show interalveolar fibrosis. A similar appearance is found in cases of fibrotic thickening of the septa, the latter probably originating in an earlier acute interstitial pneumonia.

Cuffing Pneumonia

This common type of pneumonia has also been described (Jarrett, *et al.*, 1953; Jarrett, 1954 *a* and *b*; Jarrett, *et al.*, 1954) but much work remains to be done on it.

Clinically, the disease may be subacute with coughing and varying degrees of respiratory distress or acute with dyspnœa, emphysema and pulmonary œdema; the clinical picture resembles that of parasitic bronchitis but it is found in young calves reared indoors as well as in older animals.

The ætiological specificity of the disease has not yet been proved but there appears to be a definite correlation between the stage of development of the lesions and the symptoms. The former are characterised by the appearance in the peribronchial area of excess lymphoid tissue containing the structural elements of lymph nodes. i.e., reticulin framework, sinuses and " Flemming centres." This process may continue until the affected bronchi are enclosed in a lymphoid sheath (Figs. 19 and 20) which, as it expands, causes compression collapse of alveoli (Fig. 19) and, by infiltration of the bronchial wall, bronchial collapse (Fig. 20). It is also possible that the replacement of the bronchial muscle and elastic tissue by lymphoid cells leads to fixed patency of these tubes, the three factors, alveolar collapse, bronchial stenosis and fixed patency each contributing to respiratory embarrassment. Acute inflammatory changes are usually, but not always, absent from the alveoli.

This pneumonia has been transmitted serially to susceptible calves by suspensions of lung and mediastinal nodes from both field and experimental cases.

There are morphological similarities between this condition and virus pneumonia of pigs, grey lung virus disease of mice, cotton rat pneumonia and spontaneous pneumonitis of guinea-pigs. Before postulating a virus etiology for the calf disease, although such might be the case, it is well to recall that in the porcine and murine diseases no direct correlation has been made between

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the lymphoid hyperplasia and viral stimulation of these cells, although Niven (1950) has shown that when Aureomycin is administered to mice with grey lung disease the disappearance of demonstrable virus from the lung coincides with the resolution of the lymphoid aggregates. The possibility of concurrent bacterial infection or some type of immune response has still to be investigated in relation to the lymphoid proliferation.

Pulmonary Aspergillosis

" Aspergillotic " pneumonia is well known in the human subject, in domestic poultry and in penguins. No account has appeared in the literature of the pathology of the disease in cattle; the latter has closer affinity to the human than the avian types. One case is described to illustrate the condition.

Subject. Ayrshire heifer calf aged four weeks.

History. The calf was ill for three weeks; during that time it had shown loss of condition, poor appetite and dullness but no respiratory symptoms had been noticed. The rest of the calf herd were suffering, some from diarrhœa, others from persistent mild coughing. There were no records of rectal temperature. Antibiotics had been employed on the farm but there was no information regarding this particular animal.

Post-mortem findings. There was patchy consolidation of the anterior lobes and the anterior strip of the diaphragmatic lobe of the left lung. Scattered throughout the consolidated lobules were miliary white nodules which did not appear to have any anatomical relationship to the bronchi. The right lung showed similar changes involving the whole of the apical lobe, the middle third of the cardiac lobe, the anterior half of the diaphragmatic lobe and the dorsal half of the intermediate lobe. In addition, the cardiac lobe showed acute interstitial pneumonia.

Microscopic appearances. Scattered throughout the lung parenchyma are many focal lesions (Fig. 21) which have no apparent anatomical localisation within the lobule. The most highly-developed nodules consist of a central deeply basophilic area which appears to consist of closely-packed pyknotic nuclei and fungal mycelia, part of which have undergone necrosis (Fig. 21), and a zone immediately exterior to this consisting of a light infiltration of neutrophils and macrophages intermixed with a heavy branching mycelium (Fig. 22). External to this again is a ring of collapsed alveoli in the walls of which are many large, pale " septal cells " which form the greater part of this zone and often contain fragments of fungus. Mycelia can also be seen penetrating the alveoli surrounding the nodule. Other small nodules are present which consist of foci of swollen septal cells containing fungal elements. In a few places necrosis has taken place so that almost the only recognisable formed elements are fungal. The mycelia vary in staining reaction, some being basophilic and some eosinophilic; all are stained by the periodic-acid-Schiff method. A moderately severe interstitial pneumonia is present in the right cardiac lobe without evidence of fungal elements being involved.

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Aspiration Pneumonia

This type of pneumonia occurs in all species and the lesions are usually relative to the nature of the fluid aspirated. However, it is thought worth while describing the following two cases since they occured under conditions which often obtain in the field.

Two calves had been bought in a market and housed in isolation boxes. They had probably been suckled since great difficulty was encountered on attempting to pail-feed them. Examination of their mouths did not reveal any lesions of diphtheria. An inexperienced stockman immersed their noses on several occasions to try to make them drink. They died after a febrile illness lasting 24 to 36 hours.

Post-mortem findings. Lesions were confined to the lungs. The greater part of the right apical lobe and smaller patches from half-inch to one inch diameter scattered throughout the other lobes, were dirty yellow in colour, non-crepitant and friable; they were obviously areas of coagulative necrosis. The bronchi around the necrotic areas exuded a dirty blood-tinged fluid. The unconsolidated parts of the lungs were congested and the bronchial nodes were hyperæmic.

Microscopic appearances. The affected areas vary in size from lesions involving only a few alveoli to foci encompassing several lobules; a small focus, destroying about one-third of a lobule is illustrated in Fig. 23. The lesion consists of an area of coagulative necrosis, in which the " ghost " outline of tissue components can be seen, surrounded by an irregular band of alveoli filled with polymorphonuclear leukocytes. The alveoli outside this zone show partial collapse, mural congestion and a light infiltration of polymorphs and macrophages. Where the lesion involves a septum, dilation, thrombosis and necrosis of septal lymphatics occur. Fig. 23 also shows the lesion extending into a respiratory bronchiole of an adjacent lobule.

Pneumonia Complicating Calf Diphtheria

In some cases of calf diphtheria the inflammatory process spreads to involve the lungs. In those studied personally the basic pattern is a severe bronchopneumonia although involvement of septa and subsequent interstitial pneumonia is common. The severity of the lesion varies from lobule to lobule. In some (Fig. 24) the bronchial epithelium is intact and the surrounding alveoli are heavily infiltrated by polymorphs although numerous alveoli have undergone necrosis. Other lobules show almost complete coagulative necrosis of bronchi and alveoli with loss of staining affinities and scanty cellular infiltration. Pleurisy is present when superficial lobules are involved.

Pulmonary Tuberculosis

The various types of pulmonary lesion in this condition are well known. In the district from which the material on which this study is based was obtained, tuberculosis is almost non-existent in calves and there was no opportunity to make a detailed examination. It is included for completeness of classification.

"Larval Pneumonia"

In some cases of parasitic bronchitis a very marked reaction to larvæ in the alveoli is seen. This has been described elsewhere (Jarrett, *et al.*, 1954) and, briefly, consists of varying numbers of *D. viviparus* larvæ and eggs in a lobule each surrounded by one or more giant cells of the "foreign body" type. The latter are commonly found in calf pneumonias and have a homogeneous cytoplasm and up to 40 nuclei. When they lie free in alveoli the nuclei are arranged peripherally, as in a Langhan's type cell; but when they are attacking larvæ these macrophages are applied intimately to the body wall of the parasite with consequent irregularity of their outer border and nuclear distribution (Fig. 25). More than one such cell may be attempting to engulf a single larva.

In some lobules this process may be so marked that massive cell death, both of larval and host tissue, takes place, giving rise to foci of parenchymal and larval detritus which have lost normal staining affinities, leaving only a "ghost" pattern. It is possible that this constitutes a suitable nidus for bacterial growth.

While the above conditions constitute the calf pneumonias proper which have been studied by the writer, it is considered worth while describing certain other lesions of the lung which cause interference with normal respiratory function.

Lesions Caused by Previous Bronchial Damage

(1) "Bronchial Ingrowths." These polypoid projections are often seen in lungs which have previously been infested with *D. viviparus* (Jarrett, *et al.*, 1954). They are essentially similar to the "chronic proliferative bronchitis" of the human child (Engels, 1947) which is thought to be a sequel of bronchial trauma. They consist of finger-like processes of connective tissue covered by bronchial epithelium which grow into and along the lumina of small bronchi and bronchioles. They often approximate in diameter to the lumen of the parent tube with obvious obstructive effects.

(2) This is peribronchial epithelialisation and inter-alveolar fibrosis as described above (v. "Other epithelialising pneumonias").

Pulmonary Abscesses

These are commonly found at autopsies and are often responsible for the unthriftiness of survivors from outbreaks of pneumonia or from "navel-ill," especially if the common sequel of fibrous adhesions to the parietal pleuræ is present.

Three cases are described to illustrate different varieties.

Case 1.

Subject. Ayrshire heifer calf aged 6 weeks.

History. The calf had been noticed to be ill for two weeks. The only symptoms reported were wasting and inappetance. The temperature was normal, there was no diarrhœa and signs of respiratory disease were said to be absent.

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The animal was slaughtered because of the wasting; several other calves in the herd were suffering from pneumonia.

Post-mortem findings. On opening the thoracic cavity, a large sac was found immediately behind the pericardium, extending from slightly to the left of midline to the right thoracic wall. This sac was connected, by dense adhesions, to the left lung, the diaphragm, the pericardium, and to the right parietal pleura, and it was continuous with the anterior lobes of the right lung. The wall of the sac was 1 cm. thick and composed of well-developed fibrous tissue, lined by a layer of necrotic debris; the cavity was filled with over 2,000 ml. of greyish-red, blood-tinged pus containing a few creamy necrotic or inspissated fragments.

In its lower part the sac had a thick wall as described above; near its dorsal end it was loculated, the divisions being mainly organised blood vessels. The long axis of the cavity turned from vertical to horizontal, running as far forward as the upper part of the cardiac lobe. The remainder of the lung did not seem to be affected in any way. This was confirmed histologically. The pericardium was adherent to the abscess wall and in that area showed a plastic pericarditis surrounded by strong fibrous adhesions to the epicardium. The rest of the pericardium was normal.

This lesion was tantamount to solution of a complete lobe and apparently did not cause any flagrant clinical signs. Another strange feature was the absence of pneumonia in the adjacent lung tissue. No evidence of the origin of the process was found.

Case 2.

Subject. An Ayrshire heifer calf of undetermined age.

History. No detailed history was furnished, apart from the fact that the animal was slaughtered as a "wasting bovine." The calf was stunted in growth, the head being large in relation to the rest of the body. The coat was staring and rough, the abdomen tucked up and the perineum soiled with fæces and denuded of hair.

Post-mortem findings. The left cardiac, the left diaphragmatic and the right cardiac lobes were united to the adjacent areas of the parietal pleura by strong fibrous adhesions which could not be broken down without stripping the pleura from the thoracic wall. These areas corresponded to abscesses in the substance of the lung. Several other abscesses were present, all lobes being affected except the left apical. The abscesses had thick fibrous walls and contained viscid light green pus. The adjacent lung tissue was dark brown and collapsed and the septa were thickened and prominent. Active pneumonia was absent. The regional nodes were enlarged, pale and hyperplastic. There were no abscesses in other organs; the umbilicus was healthy.

Microscopic appearance. Each abscess wall consists of concentrically arranged, heavily collagenised tissue. The innermost layer is of fibrinoid necrosis; immediately subjacent to this is a narrow area which is lightly infiltrated with plasma cells, lymphocytes and polymorphs. There is no pneumonia in the surrounding tissue.

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Case 3.

Subject. Ayrshire heifer calf aged about 10 days.

This case was one of "navel ill" or suppurative omphalophlebitis. Briefly, this case showed: (1) an abscess involving the tissue around the umbilical ring, (2) suppurative thrombosis of the umbilical vein, (3) multiple hepatic abscesses, (4) suppurative polyarthritis, and (5) pulmonary abscesses. The pulmonary abscesses were scattered throughout every lobe of the lungs and ranged in size from miliary to 1 in. diameter. The lungs were difficult to handle at autopsy as a result of the number of abscesses; the latter had no obvious walls and, since they consisted of liquefied tissue, the lobes tended to break when the organs were lifted. The pus was non-mucoid but contained numerous necrotic flecks. The immediately surrounding lung tissue was congested. On slitting the bronchi, some seen to contain purulent fluid. The abscesses were not obviously related to the bronchi.

Microscopic appearances. The abscesses are composed of a central area containing polymorphs in various degrees of degeneration and liquefied tissue debris in which no trace of former structure can be seen; surrounding this is a zone of alveoli containing polymorphs and fibrin and showing evidence of necrosis. Exterior to this the alveoli are irregularly invaded by polymorphs and foamy hæmorrhages. There does not appear to be any anatomical relationship to either septa or bronchi, although many of the latter contain inflammatory debris.

Bronchiectasis

During the course of an investigation into the epidemiology of parasitic bronchitis involving the examination, at a knackery, of several thousand lungs from cattle of all ages, it became obvious that bronchiectasis is an important and little recognised condition in cows leading to their rejection from commercial herds because of continued poor condition. It seems possible that many of these cases have their origin in calfhood pneumonia. Three cases have been chosen to illustrate the condition.

Case 1.

Subject. Ayrshire female calf of unknown age but obviously stunted in growth and being about the same height as a calf of two to three weeks of age.

History. All of the calves on the farm were showing persistent coughing, with an occasional animal developing an acute pneumonia. On account of its poor condition, this calf was slaughtered for diagnostic purposes. There was no history of purulent or fœtid nasal discharge.

Post-mortem findings. Lesions were confined to the right apical lobe, which was dark brown in colour and completely collapsed. The septa showed fibrous thickening and the bronchi were grossly dilated and bulged from the surface of the lung. This gave the lobe the appearance of several tubes of constant diameter separated by thin bands of fibrous tissue. On section, the bronchial walls were

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thickened and fibrous and the lumina were filled with viscid mucopus. The bronchial nodes were grossly hyperplastic.

Microscopic appearances (Fig. 26). The lumina are filled with pus in which little cytological detail can be distinguished. The bronchial epithelium is of low cuboidal type and lines a wall thickened by fibrosis and mildly infiltrated with a few macrophages, lymphocytes and plasma cells. There is no evidence of hyperplastic lymphoid activity in the walls or peribronchial areas. The alveoli are completely collapsed and do not contain any inflammatory cells. The septa are thicker than normal, due to an increase in fibrous tissue. The process does not appear to be an active one.

Case 2.

Subject. Ayrshire heifer calf aged 5 weeks.

History. This calf was one of several which died of cuffing pneumonia in an outbreak involving most of the calves in the herd.

Post-mortem findings. The lungs showed the lesions of cuffing pneumonia, but in addition there was bronchiectasis of the right apical lobe. The bronchi were not dilated so markedly as those in the preceding case, but the process was involving the smaller as well as the larger bronchi and this gave the lobe a more reticulated appearance.

Microscopic appearances. The bronchial and bronchiolar lumina are filled with degenerated pus. The epithelium is of the low columnar type. The main feature is the presence, in the peribronchial area. of lymphoid cuffs containing large " germ centres." There is surrounding alveolar collapse and some septal fibrosis. Acute inflammatory changes are absent. This appearance approximates to that of human follicular bronchiectasis. It seems reasonable in this case, however, to relate the bronchiestasis primarily to the cuffing pneumonia.

It is worth while noting that the right apical lobe of the ox is supplied by a bronchus which arises in the trachea several inches anterior to the bifurcation of the bronchi and that this bronchus descends almost vertically from its point of origin. It is possible that bronchial drainage from this lobe is inferior to that of the other lobes.

Case 3.

Subject. Ayrshire heifer calf of unknown age; probably about 10 weeks.

History. This calf was one of several in a herd which died of cuffing pneumonia. The history was typical of that disease.

Post-mortem findings. The apical lobes showed the lesions of cuffing pneumonia. At the posterior end of the left main dorsal diaphragmatic bronchus there was a saccular dilatation filled with pus. The dilatation was 2 in. broad and 1½ in. long and enclosed by a thin flaccid wall. There was no surrounding pneumonia and no obstructive lesion proximal to the dilatation.

Microscopic appearances. The wall of the bronchus has lost its epithelium and is lined by a thin layer of "fibrinoid" material subjacent to which is relatively

vascular fibrous tissue with a moderate infiltration of plasma cells and macrophages. There is no associated lymphoid hyperplasia or pneumonia.

No reasonable explanation of the cause of this lesion was found. It is possible that a foreign body had been present and was subsequently discharged.

Emphysema

Emphysema is a common finding at autopsies on cattle which have shown dyspnœa. Its presence and approximate extent are recognised easily on clinical examination. It is found probably most frequently in cases of parasitic bronchitis.

Although both vesicular and interstitial emphysema are found usually, the latter is most pronounced and is probably responsible for the majority of the deleterious effects.

Grossly, the degree of emphysema varies within great limits, the following stages being seen: (1) A small amount of air is present in the perilobular septal tissue. This causes an exaggerated delineation of the lobular pattern over a varying area. (2) The air has increased in amount so that the lungs do not collapse normally when the thorax is opened. The affected lobes crackle to the touch and the appearance is that of "islands" of parenchyma surrounded by raised tubes of aerated fibrous tissue. When œdema supervenes the fluid may coagulate in these areas giving the lobules the appearance of being set in a gel. (3) The septal tissue components become disrupted so that large air bullæ several inches in diameter are formed. (4) The air travels to the mediastinal tissue, and via the septal lymphatics, to the broncho-mediastinal nodes. The gas may then "track" to the thoracic inlet and escape to the subcutaneous tissues of the brisket and shoulders where it can be palpated during life.

Microscopically, there is separation of the fibrous components of the septa and pushing apart of adjacent lobules. A rather peculiar finding is the obvious aeration of the septal lymphatics.

The pathogenesis of interstitial emphysema is usually regarded as originating in rupture of alveoli into the septa. For several reasons this is thought not to be the mode of development in at least some cases. Interstitial emphysema is commonly found where there is no obvious vesicular enlargement or rupture and where the alveoli are consolidated and contain no air. It may be argued against these objections that the rupture has occurred at some other site in the lung. However, the study of a fairly large number of cases has led to the following hypothesis:

The terminal bronchiole in the calf divides to give rise to three stages of respiratory bronchioles, each terminating in alveolar ducts. In some instances the terminal bronchiolar ramifications are "reflex." The terminal bronchiole runs outwards towards the septum but its respiratory bronchioles are forced to turn inwards towards the centre of the lobule or to run along its periphery. At this point only a very thin layer of tissue separates the tidal or moving air in the bronchiole from the septum. It is conceivable in pneumonia when (*a*) the alveoli are wholly or partially consolidated, and (*b*) the inspired air is under

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greater pressure than normal due to dyspnœa, that rupture takes place at this point and interstitial emphysema is established. The force of air is much greater in the terminal bronchiole than in the individual alveoli and this would account for the spread along the septa.

Although emphysema must cause embarrassment to the cardio-pulmonary axis in several ways it is probable that the most important of these is the failure of the emphysematous lung to contract normally in expiration, hence the muscular effort which produces the characteristic grunt in cattle with massive emphysema.

Pulmonary Œdema and Hyaline Membrane Formation

Pulmonary œdema is a well-recognised condition in all animals and it is now known that several different mechanisms may be responsible for its production. In cattle it frequently complicates pneumonia and is of especial significance in "husk." Three morphological types are encountered although these are possibly variants, in degree and severity, of one process.

(1) Alveolar œdema. In this type the lungs, particularly the diaphragmatic lobes, are heavy and "waterlogged." The organs are smooth, shiny, tense and non-crepitant. When an incision is made and pressure applied to the lobe, fluid runs freely and uniformly from the cut surface. Microscopically, the alveoli are filled with a pale eosinophilic and homogeneous precipitated fluid. Fibrin deposition is scanty and cellular infiltration absent unless an acute pneumonia is superimposed on the œdema.

(2) Interstitial œdema. Here the œdema fluid is present in the septa and causes an exaggerated delineation of the lobules. The fluid in the septa is often gelatinous.

Microscopically. the fluid is present both between the fibres of the interstitial tissue and in the dilated lymphatics. Inflammatory phenomena are absent. It is not at present known whether this is a primary lesion or an œdema occurring in tissue spaces which have been previously diluted by emphysema.

(3) Hyaline membrane formation (Fig. 27). This lesion, which is of great importance in the ox, has been described and discussed elsewhere (Jarrett, *et al*, 1954) and only a brief account is given here. In many cases where the three factors, anoxia, dyspnœa and cardiac failure have been present, e.g., in "husk," pulmonary œdema of a peculiar type develops. In addition to alveolar œdema, an eosinophilic structureless hyaline membrane is deposited in the terminal branches of the air-conducting system, particularly in the alveolar ducts. This membrane by occluding the orifices of many alveoli increases the anoxia and initiates a "vicious circle" of changes leading to more œdema and membrane deposition, etc. It is found in the human subject in a wide variety of diseases and it is now certain that it is not confined to allergic conditions as was once postulated. It cannot be accepted, for example, that the finding of this lesion in parasitic bronchitis indicates "allergic husk" since it can be produced by a single dose of larvæ in a young and previously unexposed calf.

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The nature of the hyaline material has not yet been determined. It is certainly not typical fibrin from which it differs in staining reactions and it is often referred to as "albuminoid." In a condition with similar histological changes, parturient aspiration asphyxia in the human infant, Wagner (1954) has indicated that it is similar to endogenous mucus in staining reactions and has inferred from this that the membranes are of mucoid origin. This has yet to be proved in the other conditions showing this lesion.

Discussion

From a study of the changes described above it appears that calf pneumonia can be subdivided into several distinct types and to these can be added some conditions which, while not pneumonic, are important in any consideration of pulmonary disease in the bovine subject. For the greater part etiological factors have not been emphasised as the present intention is to establish a classification based on histological appearances (Table I). An initial subdivision is made on the basis of the general type of inflammatory reaction occurring, i.e., whether it is proliferative or exudative. Some of the former group, in medical literature, are often described as "atypical" pneumonias or pneumonites but this terminology is hardly applicable to the pneumonias of the ox since they are as common as, if not commoner than, the "typical" varieties. A third main division diverges slightly since it is based on etiology where the latter is obvious on morphological grounds. Further subdivisions are made on considerations of the site and type of reaction within the three primary groups.

Summary

The histological appearances of a number of different types of pneumonia and related pulmonary diseases of the calf are described and a classification of pulmonary disease in this animal is suggested on the basis of these morphological changes.

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KEY TO ILLUSTRATIONS

Fig. 1. Focal lesions of alveolar walls in collapsed lobules from a case of "white scour." H. & E. x 35.

Fig. 2. Increase of cells in alveolar walls; early œdema and infiltration of alveoli; dilatation of septal lymphatics. H. & E. x 120.

Fig. 3. Early inflammation involving alveoli in a case of "white scour." H. & E. x 100.

Fig. 4. Acute purulent broncho-pneumonia. H. & E. x 35.

Fig. 5. Mononuclear cells in alveoli in broncho-pneumonia. H. & E. x 410.

Fig. 6. Multinucleated giant-cells in alveoli. H. & E. x 125.

Fig. 7. Bronchial lumen filled with inflammatory debris; necrosis of part of bronchial wall. H. & E. x 50.

Fig. 8. Bronchiolar lumen filled with debris and with the mural structures still recognisable. The surrounding alveoli are relatively unaffected. H. & E. x 60.

Fig. 9. Bronchial node. Medullary sinuses filled with macrophages and strands of fibrin. H. & E. x 180.

Fig. 10. Interstitial pneumonia, stage 1. Dilatation, thrombosis and infiltration of subpleural lymphatics. H. & E. x 60.

Fig. 11. Interstitial pneumonia, stage 2. H. & E. x 35.

Fig. 12. Interstitial pneumonia, stage 3. H. & E. x 100.

Fig. 13. Interstitial pneumonia, stage 4. H. & E. x 35.

Fig. 14. Interstitial pneumonia, stage 4. H. & E. x 120.

Fig. 15. Interstitial pneumonia, stage 5. H. & E. x 35.

Fig. 16. Interstitial pneumonia, stage 5. H. & E. x 8.

Fig. 17. Inclusion body pneumonia. Epithelial giant-cell formation in respiratory bronchiole. H. & E. x 410.

Fig. 18. Diffuse epithelialisation of alveoli. H. & E. x 95.

Fig. 19. Cuffing pneumonia. Peribronchial lymphoid cuff causing collapse of alveoli. H. & E. 30.

Fig. 20. Cuffing pneumonia. Longitudinal section of bronchus with germinal centres in sheath of lymphoid tissue. H. & E. x 35.

Fig. 21. Aspergillotic focus at periphery of lobule. H. & E. x 35.

Fig. 22. Branching fungal mycelia in aspergillotic focus. Periodic acid-Schiff x 500.

Fig. 23. Aspiration pneumonia. Coagulative necrosis with surrounding inflammation: expansion of process to terminal bronchiole of adjacent lobule. H. & E. x 35.

Fig. 24. Necrotising broncho-pneumonia in calf diphtheria. H. & E. x 35.

Fig. 25. First-stage larva of *Dictyocaulus viviparus* being attacked by multinucleated phagocytes. H. & E. x 410.

Fig. 26. Tubular bronchiectasis. Old muco-pus in lumina; alveolar collapse; septal thickening and fibrosis. H. & E. x 8.

Fig. 27. Hyaline membrane deposition in alveolar ducts. H. & E. x 90.

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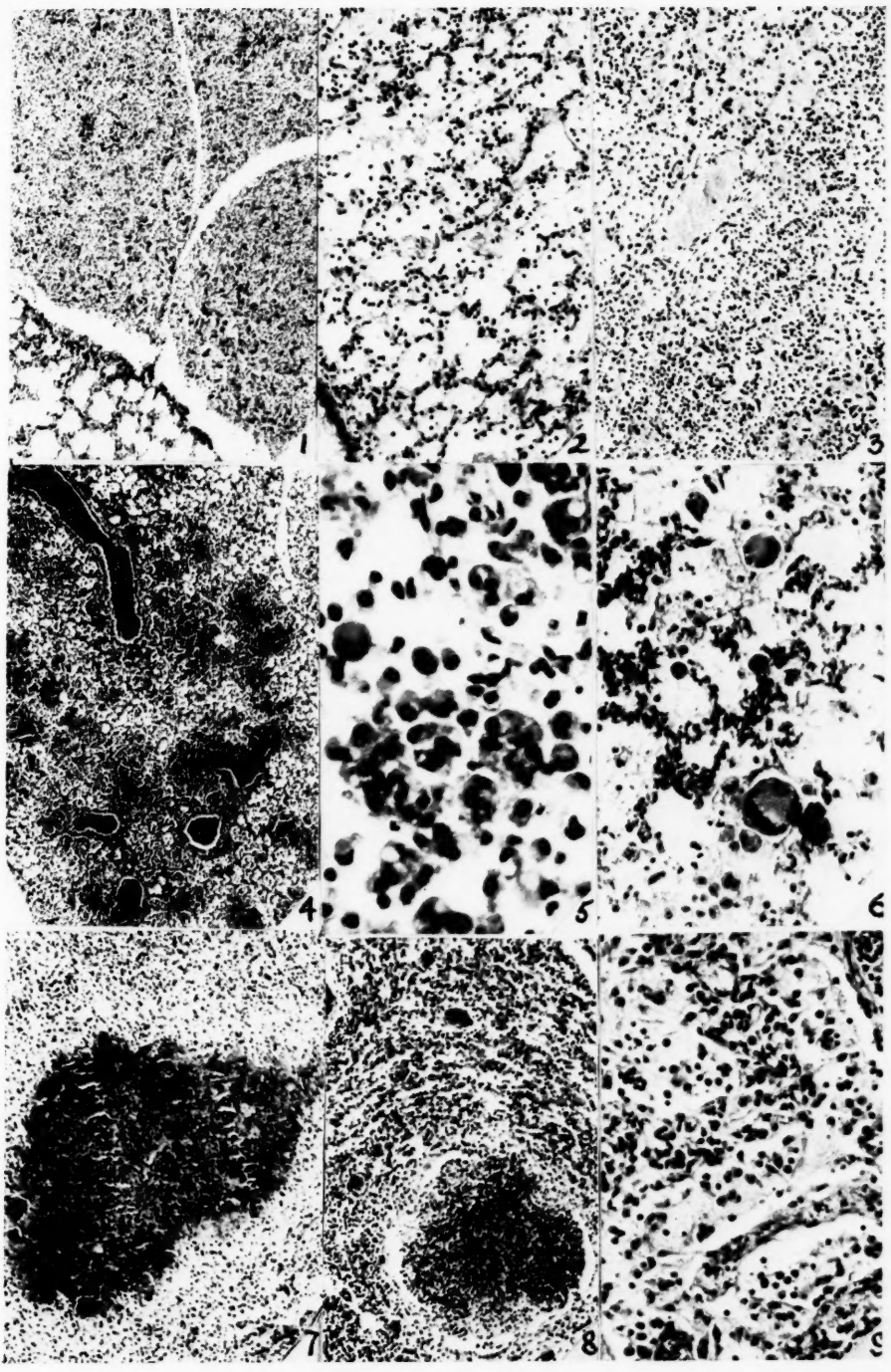
PLATE 1



(*Article by Jarrett, page* 431)

PLATE II

(*Article by Jarrett, page* 431)

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PLATE III

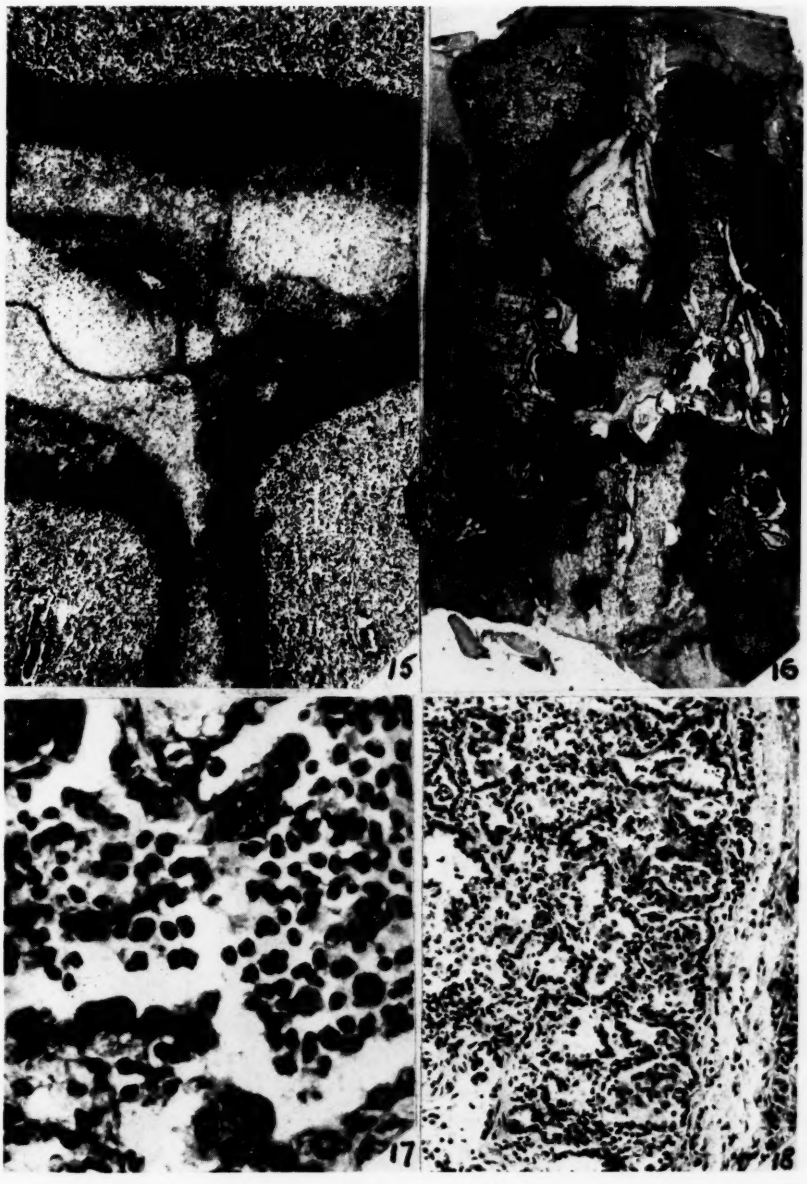

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PLATE IV

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MYCOTIC ABORTION IN CATTLE

A Case Record and a Review of the Relevant Literature

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AMONGST the various causes of abortion in cattle, mycotic infection of the fœtus, of the fœtal membranes, or of both, has been incriminated in a few reports. It is the purpose of this paper to present a probable case of mycotic abortion and to discuss various aspects of this interesting disorder in the light of present knowledge on the subject.

Case Report

The abortion occurred in the fourth month of gestation in a 6-year-old "Portuguese Frisian" from a herd of 185 cows regarded as free from *Brucella* infection. The cow had been inseminated artificially several times and aborted at the fifth month of the previous pregnancy. The fœtus was sent to the laboratory without the placenta and did not show any macroscopic lesions.

Examination was carried out by making duplicate cultures on blood-agar and Albimi-Brucella-agar* of (*a*) abomasum contents, (*b*) spleen, (*c*) liver, and (d) brain. Several tubes of Thiol medium (Difco) were seeded with (a) and (d) for *Vibrio fœtus*. One set of Petri dishes was incubated at 37° C. in normal atmosphere and the other set, together with the Thiol tubes, in jars with 10 per cent of CO_2. After four and eight days of incubation, all the cultures were negative regarding, *Brucella*, *Vibrio fœtus* or other pathogenic bacteria associated with sporadic abortion. However, the dishes smeared with the abomasum content showed colonies of a fungus which is described below. Cultures of the same material were repeated three times in ordinary nutrient-agar and colonies of the same fungus were always present in great numbers.

Two guinea-pigs inoculated subcutaneously with an emulsion of the fœtus's organs were killed after six weeks and no *Brucella* infection was present in them.

Properties of the isolated fungus. Colonies spread rapidly on dextrose (2 per cent) yeast-extract (0.5 per cent) peptone (1 per cent) agar, forming a folded mat of mycelium in the superficial layers of the medium. The mycelium was initially white, but soon formed a yellow pigment. Short aereal hyphæ were formed, bearing large globose, dark brown heads. These heads were responsible for the almost black appearance of the colonies (Fig. I).

Microscopical examinations showed the heads to be conidal fructifications of the Aspergillus type. Conidiophores were thickly walled, smooth, uncoloured and unseptate. Vesicles were mostly globose, thickly walled, yellowish brown 50 to 60 μ in diameter. Sterigmata were in two series. Primary sterigmata

* A medium especially suitable for the growth of *Brucella* and other fastidious organisms, prepared by Albimi Laboratories, Brooklyn 2, U.S.A.

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measured 5, 5 to 6, 5 μ x 25 to 35 μ; some heads, especially in the periphery of the colonies, had much shorter primary sterigmata. Secondary sterigmata showed rather uniform size, measuring $\pm$ 9 μ in length. Conidia globose, smooth or rough, brownish or yellowish, with a diameter of 3.5 to 4.2 μ. Growth at 37° C. was much better than at 25° C.

Diagnosis: *Aspergillus niger* van Tieghem (see Thom and Raper, 1945).

Review of Literature and Discussion

Smith (1920) apparently was the first to report a case of mycotic infection of a fœtus and the fœtal membranes. This case is especially important, as his material was obtained directly from the pregnant uterus, with intact seal, of a slaughtered cow. It is reasonable to suppose that contamination from extraneous material can be excluded in this case. Smith (1920) found an exudate between the wall of the uterus and the fœtal membranes. Some cotyledons were bigger than usual and showed necrosis involving the stem and point of attachment to the uterine wall (i.e., *maternal* placental tissue). The inter-cotyledonous chorion showed innumerable small, yellow-grey nodules. The fœtus had some œdema in the lungs, in the renal capsule, and in the periphery of the umbilical veins. Microscopical mycelium was observed in the necrotic cotyledons, and the amniotic fluid, as well as in the lungs and the intestinal contents of the fœtus. From the same sources pure cultures of a fungus resembling *Mucor rhizopodiformis* were obtained. *Brucella abortus* was excluded by guinea-pig inoculations. Smith (1920) presumed that the infection of the placenta had followed hematogenous spread from some primary focus, possibly in the lungs.

Carpenter (cited by Gilman and Birch, 1925) and Gilman and Birch (1925) isolated the same fungus from three fœtuses aborted at the 7th, 6th and 6½ months respectively. The abortions occurred in a herd of 90 animals, which throughout the period covered by them, showed negative agglutination tests for *Brucella abortus*. Guinea-pig inoculations with material from the three fœtuses failed to show the presence of this micro-organism.

Cultures of the fungus were obtained from the intestinal tract of the first fœtus and from the intestinal tract and the lungs of the other two. Smith (according to Gilman and Birch, 1925) compared the three strains of Carpenter and of Gilman and Birch with his own strain of *Mucor rhizopodiformis* and found them to be identical or very closely related. Gilman and Birch (1925) inoculated five pregnant cows intravenously with a suspension of the fungus. One cow aborted three weeks after inoculation and showed placental lesions very similar to those described by Smith (1920). Another animal, which was slaughtered 17 days after inoculation, was suffering from placental infection. The findings in the other three animals were negative.

Bendixen and Plum (1929) studied 17 cases of mycotic abortion. Their material consisted of placental specimens from cases of abortion, which were sent to the laboratory for routine examination. In 13 of the 17 cases, bacterial causes for abortion were ruled out by direct examination, cultures and guinea-pig inoculations. In fresh preparations and coloured sections from cotyledons, hyphæ

were observed microscopically. By cultivation, *Aspergillus fumigatus* was isolated in eight cases, *Absidia ramosa* in two cases, and both species in seven cases. Bendixen and Plum (1929) could clearly distinguish between hyphæ of the *Aspergillus* type (thin, evenly thick, markedly septated) and hyphæ of the *Absidia*-(*mucor*)-type (thick, swollen, few or no septa) in the preparations from cotyledons. In the seven cases from which both species were isolated, *either* hyphæ of the aspergillus type *or* hyphæ of the absidia type were seen. Bendixen and Plum (1929) believed, therefore, that in the latter seven cases only *one* species was originally present and that the other one constituted a post-abortion contamination. They succeeded in reproducing the disease experimentally with both *Aspergillus fumigatus* and *Absidia ramosa* by inoculating pregnant cows intravenously with a suspension of one of these fungi. The results of their inoculation experiments showed that these fungi have a pronounced tendency to infect the placenta *without* producing lesions in the other organs. Debilitated animals, however, may develop pulmonary or even generalised mycosis; the infective dose is also important. In spontaneously or experimentally infected animals it was not always possible to recognise the macroscopic changes in the placenta from cases of bacterial abortion. The Danish authors have said that the presence of cotyledons with adherent and partially necrotic maternal placentar tissue is characteristic of mycotic infection of the placenta. On histological examination this maternal tissue showed many hyphæ, necrotic and hæmorrhagic zones, with cell infiltration of polymorphonuclears, round cells and eosinophiles; the chorion was infiltrated also. In their experimental cases, Bendixen and Plum (1929) could not isolate the fungus from the fœtus. It is reasonable to presume that the infection of the amniotic fluid and of the fœtus depends upon the delay between infection of the placenta and abortion. In cases of massive placentar infection, abortion will take place before the fungus can pass the chorionic barrier and reach the fœtus either through the amniotic fluid or the umbilical veins. In less severe placentar infections, abortion may be delayed sufficiently to permit invasion of the fœtus. In very mild cases, abortion will not occur and an infected mature calf will be born (case of Bauman, 1935).

According to Bendixen and Plum (1929), 52 additional occurrences of mycotic abortion were found by Plum and Primgaard; *A. fumigatus* was isolated from 27 of them, *A. ramosa* or other undetermined *mucoraceæ* from eight others and *A. fumigatus* and a *mucoracæ* from 12; in the remaining cases no cultures had been made.

Plum in 1932 (cited by Jungherr, 1935) extended these studies to a series of 4,133 placental specimens, 1,293 of which were positive for *B. abortus,* 2,027 negative and 695 unfit for examination. Among the 2,027 specimens negative for *B. abortus,* 239 (almost 12 per cent) showed microscopic evidence of mycotic infection, and from 118 of them the following fungi could be isolated: *Aspergillus fumigatus,* 82 times; *A. versicolor,* 3 times; *A. flavus,* once; *Absidia ramosa,* 21 times; *A. lichtheimi,* 4 times; *Mucor pusillus,* 6 times; and *Rhizopus bovinus,* once.

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In 1935 Jungherr described five instances of placental alterations associated with fungi from two *brucella*-free herds.

In case 1, hyphæ of the *mucor* type were seen in sections from fœtal and maternal placental tissue; isolation of the fungus was not tried. In case 2, an intact uterus from a cow, slaughtered during the fourth month of gestation because of mastitis, was examined. The only changes observed were about 100 irregular, whitish raised areas on the amnion 0.5 to 1 mm. in height and from 2 to 10 mm. in diameter. Histologically, these plaques consisted of large, spherical or polygonal cells with comparatively small hyperchromatic nuclei. *Aspergillis fumigatus* was isolated from the amnion but, as no hyphæ were seen in the sections, and furthermore, as fœtus and placenta showed no lesions and were negative for fungi, it seems possible that mycotic infection was not present in this case, and the isolated *A. fumigatus* was a contaminant. The specimens in case 3 consisted of fœtus, placenta and uterus of a cow, which had been killed on account of habitual abortion. The only lesions found (48 hours after abortion) were in the uterus, which showed numerous hemorrhagic and necrotic "cotyledons." No hyphæ were seen in histological sections, but the following three species of fungi were isolated by culture: *Aspergillus fumigatus, A. niger* and *Rhizopus cohnii.* In this case, also, the fungi may have been post-abortal contaminants. Jungherr's case 4 is especially interesting, not only for being a true instance of mycotic abortion but also because as the same cow aborted three times and there was evidence of mycotic infection by the same species, hyphæ of the mucor type were seen in the necrotic cotyledons and *Mucor pusillus* was isolated from the placenta of the last two abortions.

Baumann (1935) (cited by Tomppert, 1940) observed a generalised mycosis in a three-day-old calf. The cotyledons were necrotic. The specimens of the causal fungus was not determined. Weidlich (1952) isolated *A. fumigatus* from skin lesions and the viscera of a five-month fetus. Recently Engel and van der Maas (1955) isolated from skin lesions of a seven-month fœtus, *A. ramosa* and *Glenospora graphii.* They did not describe the type of hyphæ seen in the lesions, therefore one is unable to decide whether only one or both species had caused the lesions.

Ainsworth and Austwick (1955) studied specimens—chiefly fœtal stomach contents—from 51 cases, seven of which were not considered representative on the grounds of gross contamination; in 41 of the 44 remaining cases a single species was obtained. *Aspergillus fumigatus* was the most frequent (63 per cent), followed by *Absidia ramosa* (12 per cent); *A. corymbifera, Aspergillus terreus* and *A. nidulans* were also isolated in a few instances.

Incidence of the disorder. The findings of Bendixen and Plum (1929), of Plum and Primgaard, and of Plum (1932) seem to suggest that mycotic abortion is a rather frequent disorder. The fact that mycotic abortion has been reported so rarely may be due to the circumstance that it is not generally recognised that the disorder may stem from a mycotic cause. It may be that many, if not most, of the isolates described by the various authors were contaminants. The grounds for this probability are the following: (*a*) In most

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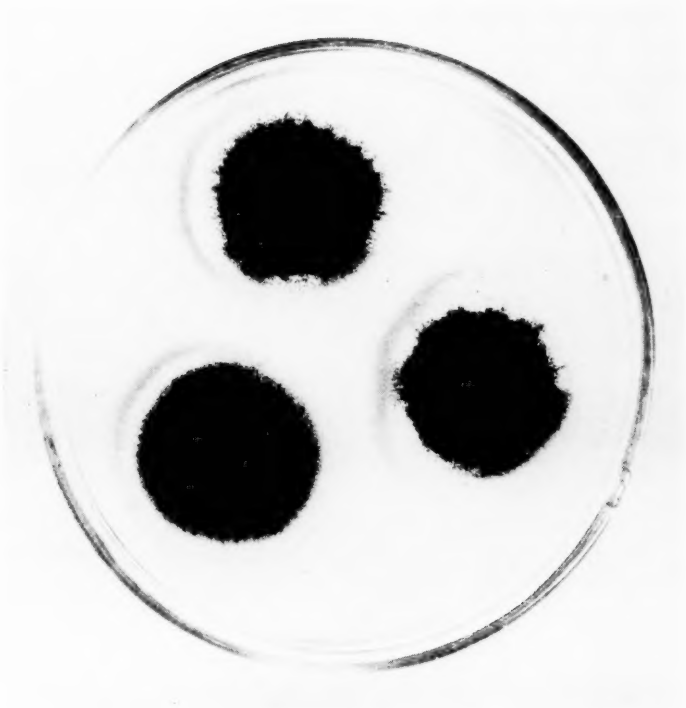

Fig 1

Aspergillus niger after five days at 37° C.

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reported instances the material was examined a considerable time after abortion had occurred (in the series of Bendixen and Plum, 39-111 hours); (*b*) the isolated fungi are ubiquitous and especially frequent on substrata (straw, hay, grain, manure, etc.) in close contact with cattle. Bendixen and Plum (1929) inoculated pieces of placenta with spores of *Aspergillus fumigatus* and *Absidia ramosa* and studied this material under various conditions. They concluded that contamination of the fœtal membranes with these fungi after birth does *not* produce a picture of mycotic infection. Hyphæ cannot be seen in fresh preparations or histological sections five to seven days after contamination. Therefore we are of the opinion that there is need for confirmation of Bendixen and Plum's work *as at the present it is not clear if bovine abortion, due to a mycotic cause, is an extremely rare or a relatively frequent disorder.*

Etiology. All the fungi so far isolated from cases of placentar or fœtal mycotic infection belong to ubiquitous saprophytic species, which can be isolated readily (with the exception of *Glenospora graphii*) from many samples of soil, grains, straw, forage products, manure, etc. These fungi become pathogenic for man and animals only occasionally.

All of the fungi which have been found associated with bovine abortion have not shown sufficient proofs of pathogenicity.

The reader interested in the full mycological descriptions and the identification of these fungi should consult the monographs of Lendner (1908), Zycha (1935) and Naumov (1939) for the genera *Absidia, Mucor* and *Rhizopus,* and the most excellent book of Thom and Raper (1945) for the genus *Aspergillus.* The species so far incriminated as causes or possible causes of mycotic abortion are now listed alphabetically and information is given regarding their pathogenic properties, in so far as this could be obtained from the extremely scattered literature:

Absidia corymbifera (see *A. lichtheimi*).

Absidia lichtheimi (Lucet et Constantin) Lendner. According to Naumov (1939), *A. corymbifera* is a synonym of this species; *Lichtheimia corymbifera* and *Mucor corymbifer* are other synonyms of *Absidia lichtheimi* (Vuillemin, 1931).

A. lichtheimi was isolated by Lichtheim (1844) (Siebenmann, 1899) from human mycoses. Christiansen and Nielsen (1929) found this species associated with mycotic lymphadenitis in swine. *A. lichtheimi* is pathogenic for rabbits (Bathelat, cited by Brumpt, 1949).

Absidia ramosa (Lindt) Lendner has been isolated from cases of human otomycosis and from the nasal mucus of horses by Lindt (1886) and by Siebenman (1889): Christiansen and Nielsen (1929) found this species in eight cases of mycosis of the lungs, spleen and mediastinal lymph nodes of swine. Zycha (1935) gives as a probable synonym *Rhizormucor parasiticus* Lucet et Constantin, which had been isolated from human sputum and was found to be pathogenic for rabbits and guinea-pigs.

Aspergillus flavus, Link. According to Thom and Raper (1945), this species may cause otomycosis (Siebenmann, 1883) and onychomycosis (Ota, 1923) in

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man occasionally and pulmonary mycosis in birds. Tscherniak (1928) cited by Tomppert (1940) isolated this species several times from cases of pulmonary and broncho-mycosis in horses. According to Brumpt (1949) *A. flavus* was found by Leszczynski and Epler and by Henrici to be pathogenic for rabbits to a considerable degree.

Aspergillus fumigatus. Fresenius has proved that this species is definitely pathogenic to man and various animals. Innumerable reports have been published on fumigatus aspergillosis of the airsacks and lungs and other organs in birds (Tomppert, 1940; Ainsworth and Rewell, 1949), of the lungs and other organs in various domestic animals (Tomppert, 1940) of the lungs, external ear and other organs in man. Henrici (1939, 1940) demonstrated the presence of a thermolabile endotoxin in the mycelium of *Aspergillus fumigatus.* This endotoxin was highly toxic when injected, but non-toxic by oral administration. Carll, Forgacs, Herring and Mahland (1955) obtained an ether-soluble toxin from corn, on which a strain of *A. fumigatus* had been grown, which is highly active when applied to the skin of rabbits, calves and horses. The same corn, given to a calf, produced acute toxic symptoms and death. According to these authors, toxins from *A. fumigatus* and other fungi may have etiological significance in hyperkeratosis (X-disease) of cattle.

Aspergillus nidulans (Eidam) Wint. This species was isolated on various occasions from pathological lesions in man and animals. Siebenmann (1889) found that *A. nidulans* was a cause of human otomycosis. Nicolle and Pinoy (1906) isolated the fungus from a case of mycetoma in a Tunisian woman. According to Thom and Raper (1945) several strains have been isolated from onychomycosis in man and one strain of this species was isolated by Pinoy (1915) from a lung affection in a monkey. Tscherniak (1928), cited by Tomppert (1940), found several cases of pulmonary and broncho-mycosis in horses, caused by *A. nidulans.* According to Brumpt (1949), several authors (Eidam, Siebenmann, Herder, Nicolle and Pinoy) found that *A. nidulans* has some pathogenicity for rabbits and rats.

Aspergillus niger, van Tieghem, is, like the other reported fungi, ubiquitous and essentially saprophytic. Its occasional pathogenicity is not proved so clearly as in that of *A. fumigatus.* Nevertheless, *A. niger* has been reported as a cause of otomycosis (Sharp, John and Robison, 1946) and ocular mycosis in man (Rosenvold, 1942; Donahue, 1950). According to Brumpt (1949), this species has been isolated on various occasions from cases of pseudo-tuberculosis in man and from a mycotic disorder of an ox and a deer. Schütz (1884), (cited by Tomppert, 1940), reported on mycosis of the airsacks and lungs in geese caused by *A. niger* and other aspergilli. He reproduced the disorder experimentally. Gorlenko (1948) found an ether-soluble endotoxin in *A. niger* which provokes a severe inflammatory reaction when applied to the skin or the conjunctiva of rabbits.

Aspergillus terreus, Thom. According to Thom and Raper (1945), this species has been isolated from a human ear in Brazil and in Nebraska from

"metastatic lesions on a cornhusker's hand and forearm." The strain isolated from the ear was described by Langeron (1922) as *Sterigmatocystis hortai.* Mackinnon (1932), cited by Brumpt, 1949), showed that it was identical with *Aspergillus terreus.* Nothing seems to be known about the pathogenicity for laboratory animals and convincing evidence is lacking that this species may become pathogenic for man or domestic animals.

Aspergillus versicolor (Vuill.), Tiraboschi, has been isolated from superficial skin lesions in man (Mirsky, 1903). Most probably it was a contaminant. So far no proof has been presented that this species has pathogenic properties.

Glenospora graphii (Siebenmann) Vuillemin has been isolated from cases of otomycosis in man (Vuillemin, 1931). According to Engel and van der Maas (1955), this species may be identical with *Monosporium lapiospermum* Saccardo. The latter fungus is a frequent cause of mycetoma in man and it has been isolated on various occasions from soil.

Mucor pusillus, Lindt. This thermophilic species is pathogenic for rabbits (Lindt, Stange, Dessy, Hoogland and Baudet, cited by Brumpt, 1949). Tscherniak (1928) isolated *M. pusillus* from cases of pulmonary mycosis in the horse, and Teutschländer (1916) from gastro-intestinal lesions also in horses. According to Brumpt (1949), Hoogland and Baudet (1932) isolated the fungus from tubercles in the liver and kidneys of a pig.

Mucor rhizopodiformis, Cohn. The identity of this fungus is not entirely clear. Naumov (1939) considers it a synonym of *Rhizopus cohnii* (see below).

Rhizopus bovinus, van Beyma thoe Kingma, is, according to Zycha (1935), a synonym of *Rh. arrhizus.* It seems that this thermophilic species has never been isolated from human or animal mycoses, with the exception of some of Plum's (1932) cases of mycotic abortion.

Rhizopus cohnii, Berlese et de Toni, is pathogenic for rabbits (Lichtheim, cited by Zycha, 1935). It was isolated from mycoses in swine by Christiansen (1922, 1929). Nielsen's (1929) *Rh. suinus* is, according to Zycha (1935), a synonym of *Rh. cohnii.* This species was isolated by Nielsen (1929) from a pig affected with generalised mycosis.

Mode of Infection. Three main ways have been considered by various authors: the digestive tract, the lungs and the genital tract.

Bendixen and Plum (1929) fed four cows with living cultures of *Aspergillus fumigatus* and *Absidia ramosa,* but did not succeed in producing infection. *Aspergillus fumigatus* and several pathogenic *mucoraceæ* can be isolated regularly from bovine intestinal contents (Van Uden and Carmo Sousa, unpublished data). On the other hand only a few cases of mycotic infection of the bovine intestinal tract (Bauman, 1935; Smith, 1920; Christiansen and Nielsen, 1929) have been reported and even in these cases the intestinal infection was not primary. It would seem, therefore, that the intestinal mucosa is extremely resistant to mould invasion and that the digestive tract can hardly be considered as a port of entry for fungi causing abortion.

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It has been shown by Gilman and Birch (1925) and by Bendixen and Plum (1929) that mycotic abortion can be produced by intravenous inoculation of *Mucor rhizopa diformis* (*Rhizopus cohnii*), *Absidia ramosa* or *Aspergillus fumigatus*. Their results not only constitute positive evidence for the pathogenicity of these fungi but reveal also a pronounced predilection of the inoculated fungi for the placenta. The fact that in most cases of experimental mycotic abortion the placenta was the only tissue involved and that at the same time the histopathological alterations of the placenta were indistinguishable from cases of spontaneous infection, strongly suggests that under natural conditions the placenta is infected by the hematogenous route from some primary focus. While, as already mentioned, the intestinal tract, most probably, is never the site of such a focus, the lungs may constitute, if not the only, the most important port of entry. In some of Bendixen and Plum's (1949) experimental cases the lungs as well as the placenta were infected. Infection of any other organ was not detected in any case. This suggests a special susceptibility of the lungs for infection with fungi which may cause mycotic abortion, and it seems reasonable to assume that in most cases the placenta is infected by hematogenous spreading from a primary lung focus. Experimental confirmation of this theory (which was already suggested by Smith, 1920) is lacking.

Rollinson and Haq (1948), on the contrary, are inclined to the view that mycotic abortion is the consequence of an ascending infection of the genital tract from outside and that coitus is a likely avenue of mycotic infection. These authors isolated *Absidia corymbifera* from the preputial washings of a bull and from the cervical mucus of a cow which had been served by that bull and had aborted in the seventh month; another cow served by the same bull aborted in the eighth month, but the fœtus was not studied mycologically. Trichomoniasis, brucellosis and tuberculosis were ruled out. As neither fœtus nor placenta in Rollinson and Haq's (1948) cases were examined mycologically, the mycotic nature of the two abortions is hypothetical.

The isolation of such an ubiquitous fungus as *Absidia corymbifera* from body surfaces (preputium, vagina) can hardly be considered as ætiologically significant. The epizootical behaviour of mycotic abortion does not favour Rollinson and Haq's (1948) point of view because bovine mycotic abortion is a sporadic disease and transmission from animal to animal would seem to be excluded. Successive abortions in the same cow "would indicate a persistence of the mycotic infection in an animal, it thereby becoming an *important disease factor* in the reproductive cycle of the *individual*, whereas mycotic infections of the genital tract are of *secondary importance*, from the standpoint of herd sanitation" (Jungherr, 1935).

Summary

A case of bovine abortion probably caused by *Aspergillus niger* is described.

The literature on bovine mycotic abortion is reviewed and various aspects of the disorder, including incidence, ætiology and mode of infection, are discussed.

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THYROTROPHIC AND GONADOTROPHIC HORMONE LEVEL IN THE BLOOD OF EGYPTIAN (FAT-TAILED) SHEEP, DURING DIFFERENT REPRODUCTIVE STAGES

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An intricate relationship seems to exist between the hormonal secretion of the pituitary on one hand and reproductive activity on the other. The activities of gonadotrophic, and thyrotrophic hormones have been found to fluctuate according to the reproductive stage. The blood level of thyrotrophic hormone in female rats and rabbits was found to attain its maximal level during œstrus (Soliman, 1952; and Soliman *et al.*, 1954*a*). It is also known that the thyroid of the female is more active than that of the male. The thyrotrophic hormone contents of the pituitaries and blood of female dogs were found to be persistently higher than those of males (Soliman *et al.*, 1954*b*). Henneman (1953) reported that the secretion of the thyroid of ewes during July (anœstrous season), is much lower than during the winter. Other studies by Kammlade *et al.* (1952) indicate that the total gonadotrophin contents of the pituitaries of ewes were the same during both anœstrous and breeding seasons.

A study of the activities of thyrotrophic and gonadotrophic hormones in the blood of female sheep during the œstrous cycle and comparing them with the hormones of the male was planned. It was expected that the results of this study would reveal some useful information which might be of some value in the successful breeding of sheep.

Materials and Methods

The sheep used in this experiment were all from the Barki breed (fat-tailed). They were bred by the Faculty of Veterinary Medicine at Giza. The experiment was conducted in June, 1954, immediately before running the ram with the flock. This is the common practice in Egypt, so that the lambing season corresponds with the beginning of the Barseem (clover) season.

Thirteen sheep of three to four years of age were used; three were males and ten were non-pregnant, non-lactating females. Five ewes were in œstrus and the other five were in diœstrus. Œstrus was diagnosed by using a "teaser ram" which had an apron and grease paint on the chest. It was allowed to run with the flock under observation. The ewes which were trailed and marked by the teaser ram were considered in œstrus and were caught immediately for collection of blood. Some of the unmarked ewes were isolated together with the teaser ram in a box for 24 hours. As both the ram and ewes showed indifference to each other, the ewes were considered diœstrous. Forty millilitres of blood were drawn from the jugular vein of each of the 13 sheep used, and collected into test-tubes

containing a few crystals of sodium citrate.) The blood of each animal was then centrifuged for 15 minutes at the speed of 3,000 r.p.m. Equal parts of plasma from animals of the same group were pooled and stored in a deep freeze until use.

Ninety unsexed one-day-old Baladi chicks were used for the assay of both gonadotrophic and thyrotrophic hormones (Evans *et al.*, 1940; and Smelser, 1938). Three groups of 20 chicks each were injected with plasma from the three experimental groups of sheep. A fourth group of 30 chicks was used as control. Chicks of the experimental groups were given daily subcutaneous injections of $\frac{1}{2}$ ml. of plasma for five days. All the chicks were killed with ether 24 hours after the last injection.) The thyroids and testes of male chicks were dissected, cleaned and weighed with a torsion balance (Table I). The data were analysed statistically using the " t " test.

TABLE I

AVERAGE THYROID AND TESTIS WEIGHTS OF MALE CHICKS TREATED WITH SHEEP PLASMA

Treatment	Number of Chicks	Avorage thyroid Wt. in Mg./100 Gm. Body Weight	Average Testis Wt. in Mg./100 Gm. Body Weight
Control	11	7.89 ± 0.55*	22.50 ± 1.20
Rams	8	10.82 ± 0.68	37.46 ± 5.80
Diestrous Ewos	7	10.70 ± 0.57	29.60 ± 3.48
Estrous Ewos	11	12.95 ± 0.68	29.42 ± 2.76

* Standard error.

Results and Discussion

Thyrotrophic Hormone Assay.

The blood of œstrous ewes was found to contain significantly higher levels of thyrotrophic hormone than that of rams and diœstrous ewes, as reflected in Table I by the increased weights of the chick thyroids. This is in agreement with previous findings by Soliman and Reineke (1954) in the rat. Œstrous

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rabbits were also found to show increased thyrotrophic level as compared with pseudopregnant and immature animals (Soliman *et al.*, 1954*a*).

The high level of œstrogen in the blood of œstrous animals is believed to be responsible for the increased output of thyrotrophic hormone, and the subsequent increase in thyroid activity. Increased uptake and turnover of radioactive iodine, denoting increased thyroid activity, was induced in rats and mice by œstrogen administration (Wolterink *et al.*, 1950; Money *et al.*, 1951; and Reineke and Soliman, 1953). This effect of œstrogen on the thyroid is mediated through the pituitary (Soliman, 1952).

A small, non-significant difference was observed between the thyrotrophic hormone levels of rams and diœstrous ewes. The level of this hormone in these two groups of animals seems to represent the normal physiological requirements for thyroid activity in sheep. This requirement is increased during œstrus. If thyroid activity is not sufficient at this time, ovulation, which usually occurs toward the end of œstrus, fails to ensue. Lehr (1952) observed that when œstradiol administration into immature rats was accompanied with methyl thiouracil, the number of animals showing ovulation decreased appreciably. Ovarian cysts were also encountered in rats with chronic hypothyroidism; their frequency was increased when such animals were given diethyl-stilbœstrol (Janes and Bradbury, 1952).

The evidence from the present experiment, together with that obtained by other investigators, seems to emphasize the importance of the role played by the thyroid during the œstrous cycle. Properly timed administration of thyroid-active material may become of some benefit in bringing anœstrous ewes into heat, or the treatment of reproductive failures caused by decreased thyroid function.

Gonadotrophic Hormone Assay.

No significant differences were observed between the levels of gonadotrophic hormone in the blood of the three groups of sheep studied. Similar results were noted by Soliman *et al.* (1954*a*) in the rabbit, and by Kammlade *et al.* (1952), who observed that the total gonadotrophin of the pituitaries of anœstrous ewes is as high as that during the breeding season.

Laplaud and Thibault (1947) reported that the injection of gonadotrophic hormone into ewes during the latter part of the œstrous cycle did not change appreciably its duration, and did not seem to affect the rate of conception. It seems that the total amount of gonadotrophin in the blood does not play an important role in controlling the œstrous cycle. It is rather the predominance of a certain fraction of gonadotrophic hormone (FSH or LH) in the blood which is associated with the different stages of the cycle. In the method of assay used in the present experiment, the relative amounts of the two fractions of gonadotrophic hormone could not be evaluated.

Summary

The levels of thyrotrophic and gonadotrophic hormones in the blood of three rams, five œstrous ewes and five diœstrous ewes were determined, using the chick

assay method. The thyrotrophic hormone level of œstrous ewes was significantly higher than that of rams and diœstrous ewes, indicating an increased requirement for thyroid activity during œstrus. The level of gonadotrophic hormone did not differ significantly among the three groups of sheep. These findings suggest the possibility of inducing œstrus in anœstrous ewes by modifying thyroid function in an appropriate manner, so that the cyclic fluctuation in its activity during the œstrous cycle is simulated.

Acknowledgment

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SOME ASPECTS OF THE REPRODUCTIVE CYCLE IN BUFFALOES

I—Gestation Period

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Introduction

In Egypt buffaloes occupy a prominent position among farm animals. They are the main source of milk. The length of the gestation is important and it was investigated on account of its importance in milking animals.

The changes associated with the œstrous cycle are normally suspended during pregnancy. Œstrus has been reported in cattle during almost all stages of pregnancy. Shalash (1956) noticed the "heat" signs among pregnant buffaloes (unpublished data). It was found, too, that "heat" might occur in the cow at all stages of pregnancy. Williams (1943) stated that from 1 to 2 per cent of pregnant cows showed œstrus. Bullard (1934) reported his observations on nine animals which exhibited œstrus on one or more occasions during a single gestation and one which showed "heat" during two gestations. The number of periods in individuals varied from one to four. Out of a total of 15 heats during pregnancy, two occurred during the first 30 days, five between 31st and 100th days, and eight between 101st and 253rd days. Donald (1943) recorded 44 "matings" during pregnancy in 36 cattle. He pointed out that the incidence of heat was probably higher. Of the 44 additional matings, 14 were during the first 30 days of pregnancy, 14 between 31 and 100 days, and 16 from 101 to 232 days. Both cows and heifers were involved.

Material

The data were collected from the records of the Bahtim Animal Breeding Station of the Egyptian Agricultural Society. The records covered 393 gestation periods of 130 buffalo-cows for the years 1936 to 1950. The gestation length was calculated with the days of service and calving excluded. All the buffalo-cows were kept under the same conditions as regards management, feeding and breeding during the period of study.

Results

The average gestation length for all animals was 316.15 days with a range of from 300 to 346 days. It was found that the gestation period in buffalo-cows which gave birth to female calves ranged between 301 and 337 days, with an average of 315.71 days. The length of pregnancy of those animals which produced male calves ranged from 300 to 346 days with an average of 316.53 days (see Table I).

The percentages of female and male buffalo calves born in 393 gestations from 130 dams were 46.56 per cent and 53.44 per cent respectively.

TABLE I

Effect of Calf Sex on Gestation Period.

Sex	Number	Average (days)	Range (days)
Male	210	316.53	300 to 346
Female	183	315.71	301 to 337
Total	393	316.15	300 to 346

By grouping gestation lengths according to season of calving (Table II) the collected data show that the gestation periods varied with time of year.

In winter the length of gestation ranged from 301 to 330 days. with an average of 318 days; in spring it ranged between 300 and 346 days, with an average of 318.08; in summer it ranged between 303 and 337 days with an average of 316.19 days; in autumn it averaged 316.27 days and ranged from 301 to 332 days.

TABLE II

Correlation between Gestation Period and Season of Calving

Season of Calving	Number	Sex	Average(days)	Range(days)
Winter	25	Female	317.8	301 to 330
	40	Male	318.15	308 to 330
Total	65	Female and Male	318.0	301 to 330
Spring	23	Female	317.82	306 to 326
	49	Male	318.21	300 to 346
Total	72	Female and Male	318.08	300 to 346
Summer	74	Female	316.89	303 to 337
	62	Male	315.35	304 to 330
Total	136	Female and Male	316.19	303 to 337
Autumn	57	Female	317.45	301 to 330
	62	Male	315.21	304 to 332
Total	119	Female and Male	316.27	301 to 332

Discussion

The normal variation of the duration of pregnancy irrespective of the season of calving in the buffalo-cow was 16 to 30 days on the average duration of 316.15 days and could be attributed to many factors. Since the duration of the diœstrous cycle is reduced by better feeding conditions, it may be that nutrition acts in a similar way in both the diœstrous cycle and pregnancy by

affecting the life of the corpus luteum. Robson (1947) states that the duration of activity of the corpus luteum of pregnancy can be prolonged beyond its normal time by the administration either of gonadotrophic hormone or of an estrogen. He adds that Snyder (1934) induced the formation of new corpora lutea in the ovaries towards the end of pregnancy by intravenous injection of gonadotrophic hormone; these corpora lutea remained active for some 16 days, during which time expulsion of the uterine contents did not occur. Hammond (1922) said that the variation in the length of the diœstrous cycle due to the duration of the corpus luteum may be normally about five days in a cycle of 20 days; since the duration of the corpus luteum in pregnancy is 14 times as long it will be seen that the variations in both pregnancy and the cycle are of the same degree. He cites Vignes (1923) who gives data which indicate that this is so for women, cycles of 30 to 40 days averaging a pregnancy of 288 days whereas cycles of 21 to 26 days averaged a pregnancy of 269 days.

Ashoub (1936) stated that the gestation period in the buffalo-cow varied from 10 to 11 months. Williams (1917) believed that variation of the gestation period is due to the fact that the fœtus can be expelled in a state of relative immaturity, and while this is no doubt true it does not account entirely for variation beyond the average time of 280 days.

Berry-Hart (1913) was of the opinion that variation in the duration of pregnancy in cows was caused by the spermatozoa injected at one heat period living and fertilising the egg shed at the next period. In women where coitus is allowed at any period of the cycle the duration of pregnancy might be affected by the period between insemination and fertilisation (Triepel, 1919) but this is only a few hours in the buffalo-cow.

In this investigation the length of the gestation periods ending in summer and autumn were shorter than those ending in winter and spring. This can be attributed to the fact that the better quality nutrients provided at Barseem would tend to shorten the length of the gestation period (Zaher and Ghanem, 1953). Another possible cause for the seasonal variation may be the differential endocrine activities during the different seasons. Wellmann (1910), cited by Hammond (1922), found that in mares there is a difference in the length of the gestation period according to the season of the year at which foaling takes place; pregnancy averaged 322 days when the births occurred in July and there was a constant increase up to May when the average duration was 346 days; he also found a similar variation in cows but to a smaller extent.

In this work it was found that the duration of gestation for male calves was longer than that of females. Ashoub (1936) stated that with the male fœtus the duration of gestation is greater than in the case of a female. Spencer (1839) according to Hammond (1922) found in shorthorn cattle that the largest number of female calves were born on the 284th day and bull calves on the 285th day. Zaher and Ghanem, 1953, found that in the mares the sex of the foal did not seem to affect gestation lengths.

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Summary

1. A study of the variation in the gestation periods of 393 buffalo-cows was carried out.

2. The duration of gestation of a male fœtus was slightly longer than that of a female.

3. The percentages of female and male calves born were 46.56 per cent and 53.44 per cent respectively.

4. Seasonal variation caused the gestation lengths preceding winter and spring calvings to be longer than those ending in summer and autumn.

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REVIEWS

DAIRY FARMERS VETERINARY BOOK, by Norman Barron, M.R.C.V.S., Ph.D. Ipswich: Dairy Farmers (Books) Ltd. Price, 21s.

THERE is a demand by the public for information on the management and treatment of animals in health and sickness. That demand used to be most marked amongst those who were interested in horses and dogs. It would appear that, in modern times, those who tend upon the dairy cow are the most avaricious in the search for knowledge. Dr. Norman Barron's book "The Dairy Farmers Veterinary Book," which was published first in 1950, has achieved the status of a "best seller." The first edition ran to six impressions and a second edition has been called for in 1956. Both editions have achieved the dignity of a "Foreword" by one who has served with efficiency and dignity as the agrestic political hierarch.

The modern farmer or herdsman wants to know the reason "why" and he does his job all the better for it and Dr. Barron has essayed to satisfy this demand. The format of the book is in logical sequence, the language is straight forward and lucid. The illustrations are profuse and good. The strip cartoons illustrating how to do this, that, or the other thing, transmit their message with great clarity.

This book will serve well the audience for which it caters and there is no doubt that it would be of value to veterinary students as a basic introduction to their clinical studies. Practitioners need have no fear that it will lessen the demand for their services. The best clients are those possessed of some sound elementary knowledge of animal husbandry in health and disease for they are able to appreciate the good dividends that can result if they collaborate intelligently with their veterinary surgeon.

VETERINARY DRUG ENCYCLOPEDIA AND THERAPEUTIC INDEX, 4th edition. Edited by H. C. Stephenson and S. G. Mittelstaedt. Drug Publications Inc., New York, 1956, pp. 374. Obtainable from London, Baillière, Tindall & Cox Ltd.

PROFESSOR STEPENSON is Emeritus Professor of Therapeutics and Small Animal Disease, at Cornell University. Doctor Mittelstaedt is Dean of the School of Pharmacy at the University of Arkansas.

The fourth edition of this quick reference guide has been enlarged. It now contains details of nearly two thousand drugs, biologicals and foods produced by eighty-seven manufacturers.

All drugs have been described impartially and the year of addition of a new preparation is indicated. As before the book is divided into three sections; firstly details of the products, secondly, a manufacturers' directory and index, and thirdly, a therapeutic index.

With the diversity of trade names applied to similar products of such a multiplicity of manufacturers, this book is obviously essential to every practising veterinary surgeon in the U.S.A. In Great Britain it is of only general interest to the practising veterinary surgeon, but it is extremely useful to those engaged in teaching or clinical research, and to manufacturers.

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NEUROLOGIC EXAMINATION OF THE DOG WITH CLINICOPATHOLOGIC OBSERVATIONS, by John T. McGrath, V.M.D. London: Henry Kimpton. Price, 37s. 6d.

IT is strange that although much of the information that a neurologist uses in order to diagnose the site and nature of the lesions and abnormalities which affect the nervous system of man was elucidated by the study of the experimental dog or cat, that information has not been accessible in ready manner to veterinary surgeons who are called to deal with these matters in everyday practice.

The author has attempted to set forth, and within the confines of a relatively short text, the fundamental or basic principles on which an intelligent anatophysiological examination of the nervous system of the dog can be made. He has also discussed some of the common pathological and other lesions which may offend the brain and spinal cord and which portend certain abnormal neurophysiological signs and symptoms.

He stresses the great value of a good history and the fact that certain neurological lesions are more common in some breeds than in others and that a careful evaluation of these things may indicate a probable diagnosis. I think that an observant veterinary surgeon could indicate a positive diagnosis in many instances on such evidence. In chapter 3 he deals with the physical examination which should always precede the specific neurological investigations for many abnormalities of the nervous system are reflected objectively in other parts of the body. In chapters 4 to 7 he refreshes our knowledge of the C.N.S. and the distribution, nature, and function of the cranial and spinal nerves. In chapter 8 he tells of the common reflexes that can be utilised in a neurological examination, how to recognise and interpret any departure from normal, and how such aberrations may be used to identify the site of the initial lesion. In chapter 9 the cerebrospinal fluid is reviewed. He discusses its origin and composition, how samples can be obtained, and the laboratory examination of the fluid. Myelography using contrast radio opaque media is mentioned and one is told of its value in the diagnosis and location of lesions which encroach upon the spinal canal. Chapters 10 and 11 occupy a little more than half of the book. They deal with intracranial and vertebral column pathological lesions. Numerous clinical cases are cited and the neurological signs and symptoms prognosis and treatment are discussed.

The author has collected information from many sources, and veterinary neurological students will find the extensive classified bibliography at the end of the book of considerable value, but there is much which must have come from his own searching. The illustrations are numerous, selected well, and excellently reproduced. As one who has a similar interest in veterinary neurology I admire his courage in attempting to place before his colleagues, who have not access to the relevant and voluminous literature, such a fund of information within the confines of a relatively small book. He has used language in a lucid style that all can understand. I think that he has succeeded in his task and I am sure that he will be rewarded by the interest provoked.

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NEWS

THE Committee of Privy Council for Agricultural Research have appointed Mr. R. E. Glover, M.A., B.Sc., F.R.C.V.S., to fill a vacancy in the membership of the Agricultural Research Council caused by the resignation of Professor G. R. Cameron, F.R.S., and have re-appointed Professor S. J. Watson, M.Sc., D.Sc., F.R.I.C., F.R.S.E., for a further term. Professor Watson will continue to act as Deputy Chairman of the Council.

THE Managing Committee of the International Fertility Association has appointed an apposite Committee on Animal Reproduction. Professor T. Bonadonna of Milan (Italy) has been nominated Chairman and Dr. K. McEntee of Ithaca (U.S.A.) and Professor N. Lagerof of Stockholm (Sweden) members.

The object of the Committee on Animal Reproduction is to encourage veterinarians and biologists to take further interest in the activities of the International Fertility Association, and to co-operate in the improvement of animal fertility.

THE Animal Health Trust announces that the following have accepted invitations from its President, the Duke of Norfolk, to become members of the Executive Committee:—The Earl of Northesk, Vice-Chairman of the Kennel Club and of Cruft's Dog Show; Mr. Francis S. Gentle, C.B.E., Chairman and Managing Director of the Greyhound Racing Association, Ltd.; Sir Thomas Peacock, C.B.E., Chairman of the Milk Marketing Board; and Mr. L. M. Du Pré, Vice-President of the National Farmers' Union.

NOTICES

ALLEN AND HANBURYS LTD. announce price reduction of Dapsyvet Pessaries. All orders despatched on and after Monday, September 17, 1956, will be charged as follows:—Dapsyvet Pessaries, each containing chloramphenicol 0.3 g. and dapsone 1.5 g. in a urea base. Cartons of 5 (professional), 7s. 5d. Exempt from purchase tax.

PFIZER LTD. announce that the professional price of the 1 Gm. vial of Terramycin Intramuscular has been reduced from 33s. 1d. to 29s. 7d., effective from October 1, 1956.

Publishers' Notices

THE BRITISH VETERINARY JOURNAL, with which is incorporated THE VETERINARY JOURNAL, is published monthly, and copy for advertisements should be in the hands of the advertisement manager not later than the 20th of the preceding month, if proof is required. Tel.: Temple Bar 3386.

Letters for the Journal, literary contributions, reports, notices, books for review, exchanges, new instruments or materials, and all matter for publication (except advertisements) should be addressed to the Editor.

Annual Subscription, 40s. ($6.50 U.S.A. currency, post free).